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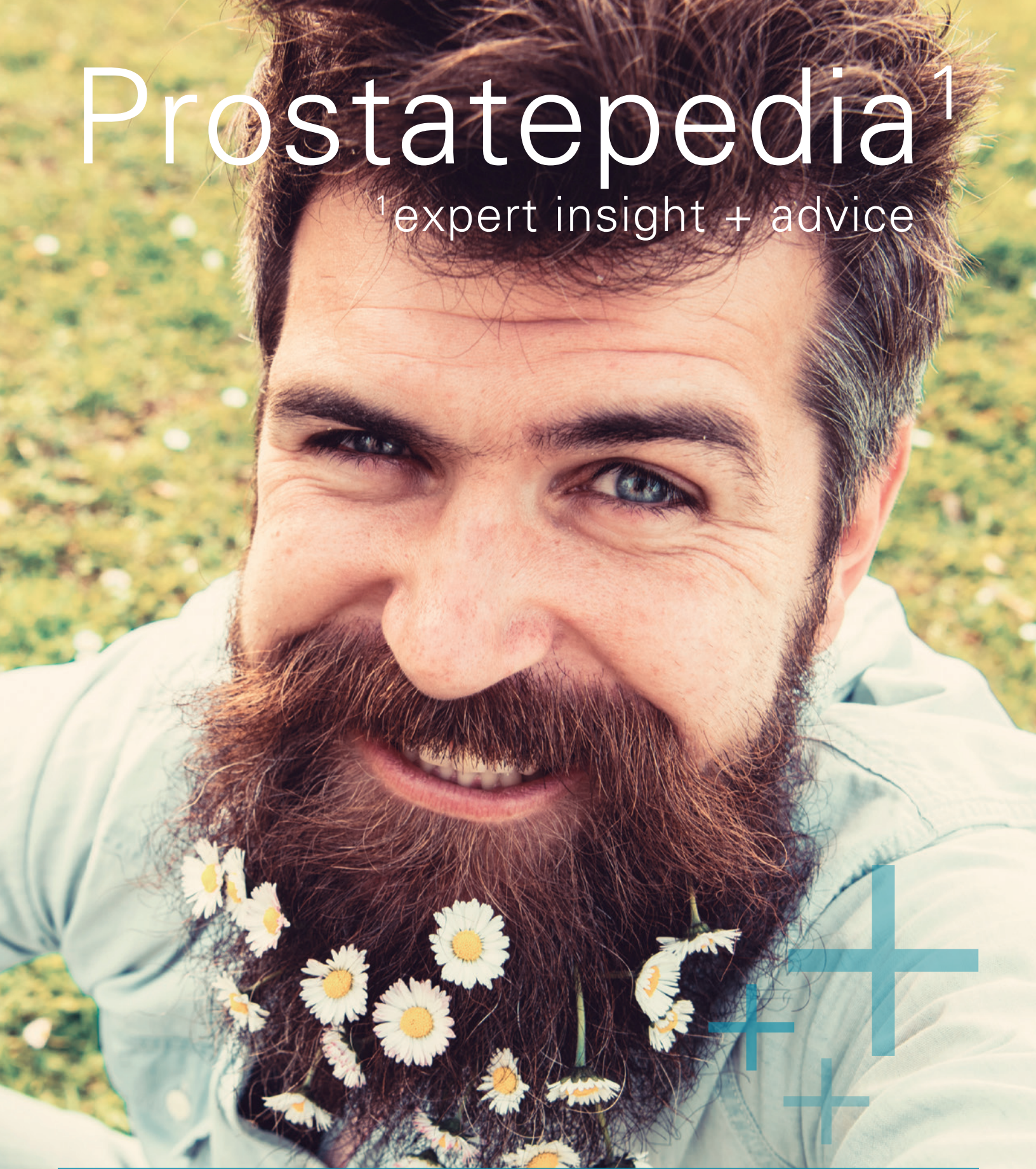

Clinical Trials

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In this issue....

In May, we're talking about clinical trials for prostate cancer patients. We also have an ulterior motive: we would love it, if after reading this issue, each and every one of you asks your doctor if there is a clinical trial that is appropriate for you. Why? Clinical trials are the only path to furthering our understanding about how and why prostate cancer occurs—and progresses—in some people and not others. It's also the only way we can develop new and better ways to treat prostate cancer.

But all of that is lofty and altruistic.

How do you, as an individual patient, benefit from joining a clinical trial? First, you may be able to access treatments, procedures, or imaging that you would not otherwise be able to access.

And even if you're on the control arm of a study, you'll get standard-of-care, which could mean drugs, scans, or procedures at a reduced cost. At the very least, when you join a trial you will be more rigorously monitored by the study team, which could lead to better outcomes for you. Studies show that patients on clinical trials tend to do better than those not on clinical trials, even if they get the same treatment.

When should you consider looking for a trial? Right after you're diagnosed. Just ask your doctor if there are any trials that are right for you. There may not be. But by asking, you're letting her know that you're interested so that, the next time she runs across a trial looking for patients like you, she'll be sure to bring it to your attention.

Once you enter a trial, make sure you let the investigators know that you're interested in the results. Of course, given both prostate cancer's long natural history and the clinical trial process, those results may not come for many years after your actual participation, but let the researchers know that you'd like to know the results once they're available.

As you'll read in the conversation with Ms. Merith Basey, too many clinical trial results go unreported in the United States and on a global scale. How can you help? As Ms. Basey points out, if you graduated from a United States university, call or write your alma mater to let them know that you'd like the administration to ensure that every trial conducted under their auspices is reported—whether those results are positive or negative.

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Rick Bangs SWOG + Clinical Trials

Rick Bangs, MBA, PMP, is the bladder cancer advocate on the genitourinary committee of SWOG Cancer Research Network (originally known as South West Oncology Group). He serves as chair of the SWOG patient advocate committee and is on the SWOG executive advisory committee. He lives in Rochester Hills, Michigan. Rick has 30 years of experience in information technology and marketing and is advising on the redesign of ClinicalTrials.gov. He is co-chair of the NCI Patient Advocate Steering Committee and serves on the NCI Cancer Care Delivery Research Steering Committee and Council of Research Advocates. Rick actively supports the Bladder Cancer Advocacy Network and Movember. He previously served on the NCI Genitourinary (GU) Steering Committee. He is a bladder and prostate cancer survivor.

Prostatepedia spoke with him about clinical trials for prostate cancer.

How did you get involved with patient advocacy in the first place?

Rick: When I was first diagnosed with bladder cancer, I sat outside the clinic, filling out forms for some clinical studies on quality of life, and I came to the decision that, regardless, some good was going to come out of my cancer.

I found out that I had prostate cancer after my surgery for Stage II (muscle-invasive) bladder cancer because, if you're a man, when they remove your bladder, they also remove your prostate.

Three years after my surgery, I went to an advocacy event held by the Bladder Cancer Advocacy Network (BCAN). At the time, they met in two major cities a year, and Cleveland happened to be one of the cities that year, which was a four-hour drive for me. I went and met the president and co-founder of BCAN. I gave her a copy of the presentation I was giving the next day at the University of Michigan bladder cancer support group. We chatted and I offered her any help.

About six weeks later, she asked me to respond to an interview by ABC News about the disparities in cancer funding. That went pretty well, so she reached out to me about a month later and asked if I would replace her as the SWOG bladder cancer patient advocate. She said she couldn't do everything that was being asked of her. I accepted, and that created a series of dominoes that led us to where we are.

What is it about patient advocacy that keeps you interested? What is it that keeps you coming back?

Rick: Being in the room where it happens, where change happens, and having the opportunity to work with really cool people on really cool projects to make a difference is what keeps me coming back. I enjoy doing that both directly in the spaces that I work in, which tend to be bladder and prostate cancer for obvious reasons, but also with my counterparts in the leadership roles that I have.

In bladder cancer, we've been on what some bladder cancer researchers once described as a "shallow plateau" for nearly a generation from a treatment point of view. That's been changing in the last few years, but it's been true for so long. For me, it's raising that shallow plateau and being part of the process.

Would you say that what it means to be a patient advocate is changing?

Rick: Yes, particularly in research advocacy, a subset of this big, broad basket of things that patient advocates do. It's amazing to see how our work is maturing.

There are things that I can do today to articulate with some specificity the work that a patient advocate does in cancer clinical trials. I can say: here's the lifecycle, here's what I can do at this stage, here's what I can do at this next stage, here's where you should involve me, and here are some other things that wrap around that from an organizational point of view. I can articulate those.

I can point to processes and expectations that didn't exist two years ago and consensus around them. I can point to training across the five stages of the clinical trial – training on how to optimize the engagement of patient advocates and maximize the value that we bring to the party. I'm not talking about training just for patient advocates, but for patient advocates, principal investigators, leadership, and other members of a study team. That was a huge hole that we chose to fill at SWOG.

We did an environmental scan and found absolutely nothing; there was no training on engaging advocates in creating and running clinical trials. We had training for patient advocates on what cancer is, what trials are, and how to review a study concept. But we didn't have any training for teams on how to more broadly engage patient advocates in the specifics of the activities that they work on.

What does SWOG do, and what is SWOG's mission?

Rick: SWOG is this amazing team of exceptionally talented people who work in one of six networks in the U.S. and Canada that make up the National Cancer Institute's National Clinical Trials Network, or NCTN. The NCTN was created by the NCI in the 1950s to test chemotherapies, which were new at the time, and it is the oldest and largest cancer clinical trials network in the country.

The whole reason that SWOG and the NCTN exists is to design, deliver, and share the results of clinical trials that will change the standard of care for patients, their families, caregivers, and partners. They're funded by the NCI, which also provides critical support and services to the NCTN, like a Central Institutional Review Board.

That's the general answer about SWOG and what they do, but it's important to think about the results that SWOG has achieved. Since it was founded in 1956, SWOG research has led to the approval of 14 cancer drugs. We have also changed the standard of care over 100 times.

One of our biostatisticians did an analysis—and it's a very conservative analysis—of how many years of human life we have saved. If somebody before a trial lived for 10 months, and now they live for 12, and if you multiply those two months times the number of people who have the disease, times the number of years since we changed the standard of care, the answer is: 3 million years of human life. That's at least how much time we've saved for patients to be with their families and do things that are important to them.

When you think about the opportunity to work on things that are that important, it's incredibly rewarding.

What kinds of trials does SWOG run?

Rick: We're typically playing in the Phase II and Phase III space, although we also do some work in the very early Phase I (first in human) space.

We focus on trials that are going to change people's lives in a significant way. That includes treatments and therapies but also prevention and survivorship. We don't shy away from those topics in our scope of the work. We do research that the pharmaceutical industry itself will not do.

We work, for example, on dose reductions. You can imagine that a company has little incentive to get patients to take less of the drug they produce.

We work on alternate sequencing; this treatment, followed by this. We might look at how we ended up with a particular sequence and whether there is a better way to do the sequence.

We work on drug combinations. Individual pharmaceutical companies may have combination drugs, and they may have partners, but we look at combinations more broadly and create some synergy between drug combinations that pharma would not have considered.

We typically take on the complex and difficult. SWOG has more than 1,000 member institutions, and some are larger academic institutions, but we also have many hospitals and clinics in rural and suburban communities. The group that works to address the rural setting also makes sure we're accounting for and addressing disparities in healthcare. We also do some work with cheaper effective

drugs that may not currently get attention or investment from pharmaceutical firms.

In the bladder cancer space, we have a shortage of an immunotherapy drug that we've been using since the late 1980s. We were on the cutting edge back then, which for bladder cancer is like an oxymoron. We began to use Bacillus Calmette-Guerin, which is related to tuberculosis, and through testing in the late 1980s at SWOG, it was confirmed to be effective for many patients. It's instilled in the bladder through a catheter. It's a biologic, so there are different strains of BCG, it's not a single drug, and it is difficult to manufacture. We have been using it for years, but now we're down to one strain in the United States that Merck makes, and they can't keep up with demand globally. We're experiencing our third shortage in seven years.

SWOG is doing a study because, believe it or not, we really don't understand how this 30-year-old treatment works, and we knew that there had been and would likely continue to be shortages, so we wanted to take care of both. We wanted to be in a position where we could address the shortages, but we also knew that there was potential to understand the mechanism of action of BCG and also potentially get better results with sequencing.

Research underlying the SWOG S1602 PRIME trial indicates, for example, that if people had a specific tuberculosis vaccination, and you waited a certain amount of time before BCG was installed in the bladder, that they got a better response than with just the installation in the bladder alone.

This is because the immune system was primed through the vaccination and built up some immunity before installing BCG in the bladder.

We're doing a trial testing a new strain of BCG with and without vaccination. I can't imagine pharma funding a trial like this. It's a low-profit margin drug, and people have walked away from it.

Yes, it could only come from an organization like SWOG. Pharma wouldn't necessarily invest in, right?

Rick: Right, because they're going after the hot, profitable immunotherapies. They're not after this 30-year-old, low-profit treatment. That's not where they'll recoup their investment.

SWOG plays an important societal role!

Rick: Yes. As Americans, we don't appreciate the return on the investment that we get from the NCI and these clinical trials. NCI pays for itself many times over. Most Americans don't even know that the research is happening, let alone that it's that beneficial.

Right, well, this kind of information rarely makes it to mainstream news, unless a sensational clinical trial either fails or is wildly successful.

Rick: Exactly.

Let's say patients reading this understand the role that SWOG and other NCTN clinical trials play in the development of new drugs for prostate cancer. But why should they consider joining a trial? What's in it for the individual man?

Rick: There are several reasons. First, anybody who's diagnosed with any cancer will find that they, too, are on a shallow plateau in terms of treatment options no matter what their diagnosis, though exactly how shallow varies by the cancer. The treatments are insufficient, have unpleasant side effects, and never work fast enough. If we want to advance the science, and if we're going to change these insufficient treatments, we've got to have clinical trials.

Second, no single clinical trial for a treatment ever studies a single question; we're always doing other studies at the same time within the clinical trial. It's like three, four or more studies for the price of one. We do the trial on the treatment, but we also learn the mechanism of how it and the cancer work, and we build up the knowledge that we need for the next set of trials. It pays off not just in terms of one clinical trial but a series of them.

Third, there are studies that demonstrate that the care that a patient gets in a clinical trial is great. Physicians who put patients on trials are very attentive and careful in their execution, going above and beyond the standard.

Fourth, giving back is another great reason for patients to join.

Last, but certainly not least, you are often given an opportunity to participate in a treatment or an intervention that may improve your cancer journey. That isn't always the case, and there's never a guarantee, which is why we do a clinical trial, but we know that clinical trials work about half the time. Some people clearly benefit from participating.

If a man understands that a clinical trial may be of benefit both to him and to society, should he start looking for a trial when his cancer has advanced

beyond a certain level, or should he start looking for one when he's first diagnosed?

Rick: I would suggest that a man check on a clinical trial no matter what his diagnosis, and, frankly, no matter what his disease.

There are clinical trials out there that span the entire lifecycle of every disease. People are doing work on prevention, early-stage disease, and late-stage disease. People are also doing work on caregiving. Partners, spouses, family, and friends are tightly integrated into the cancer journey, and there's a place for them in clinical trials too. I would suggest that people ask about clinical trials no matter their diagnosis.

How would you suggest they go about finding a trial? Should they talk to their doctor, search online, or contact patient advocacy groups?

Rick: It's always appropriate to start with a physician. The challenge is going to be the geographic dispersion of clinical trials. We know that most of them are centered in larger academic institutions and larger cities.

At SWOG and our counterparts, we have a community base that supports us, that ensures we're getting out there. But for many patients, their physician may not know about a clinical trial.

Where should you go from there? You can search ClinicalTrials.gov, which I've worked on. You can search Cancer.gov, which includes only trials that are funded by or conducted at NCI sites. You can start with those and make a list, and then you can talk to the physician about narrowing that list down.

Advocacy groups can be a great mechanism. Many of them are armed with people who are like me but even more focused on the specifics of the clinical trials and the disease settings. They can be very helpful. They know how to navigate online searches, but they also know how to work through the complex information about qualifying.

If you've found a trial, you can use ClinicalTrials.gov to find the principal investigator, and you can ask them for further information and whether you qualify. Believe me, they are happy to help.

Social networking is becoming a mechanism for people to connect, and particularly for folks with rare diseases or rare forms of common diseases. Facebook groups and web forums are good possibilities.

Don't be afraid to ask for help. If you talk to the physician and the physician says no, reach out to an advocacy group, or try to find something on ClinicalTrials.gov, or go out to a web forum or a Facebook page and ask about possibilities. NCI has a Contact Center that is based in Seattle. Don't be shy about calling 1-800-4-CANCER.

What kinds of information do they provide at the call center? Can a patient, say, call up, explain their situation, and ask for a personalized list of trials available?

Rick: Yes! The NCI Contact Center helps connect a patient with a trial – but they never push a trial. These are neutral, well-trained counselors. They will go the extra mile. I don't know what kind of success rate they have, but I know they get a large number of calls. But most people don't even know to make the call. Contact Center staff also can chat online or answer questions by email.

Are there any considerations patients should keep in mind as they look through these trials?

Rick: The first thing to remember is that we do trials because we don't have the answer. If you start searching for a trial, and you find something, you shouldn't automatically assume that it is going to be successful. You have to come at it from the perspective that it may or may not benefit you personally.

Geography and institutions matter. If you ask your doctor, and the doctor says they don't know of any clinical trials, that does not mean there aren't any at other institutions or in other places. I would not take *no* as a definitive answer from a single physician, particularly in a more rural setting.

Oftentimes there are trials that require maybe an initial visit, or an initial series of visits, and then follow-up can be done remotely, correct?

Rick: Yes, though that tends to be a little tricky. It isn't always possible. We keep trying to move in that direction. Patient advocates emphasize that as a possibility. It gets a little tricky because there are quality and recordkeeping considerations.

Convenience for the patient is certainly first and foremost, but typically specimen extractions can be complicated, even if it's blood, urine, or tissue, and activity may need to happen around and to that sample and within a certain time. There are many complexities around that, but certainly that can be possible.

I've heard that it's very difficult to find and recruit patients for trials, and that many trials don't end up fully accruing. Is that true? Why do you think that is?

Rick: Historically, a number of trials have had to close because there weren't enough patients. This is not current data, but some years back, about a quarter of trials had to close for insufficient recruitment.

We're doing much better now, but why was that the case? Some trials were not as patient-centric as they might have been, and could have been better designed, asking more interesting, more potentially significant questions. Trials were mostly in large cities and access was an obstacle. We also haven't always had exciting treatments to offer. We have more exciting things happening today. Immunotherapy is one example that's more exciting today. So trials are much better today, though we still have challenges.

Why do we still have problems recruiting patients? First, patients are not always offered a clinical trial, in part because clinical trials are not everywhere. It's not like I can just go to my primary care, emergency room, or my local clinic and say, "I'm here for the clinical trial." That doesn't happen.

There are logistical and access challenges. Patients are not always asked, and when they are, they are concerned about placebos. But we don't do clinical trials where patients get nothing instead of something that works that they would normally receive. They're going to get something, or they're going to get the alternative. We're not going to take anything away from you. That never happens, but people think it does.

There's a misconception that clinical trials are only for people who are desperate for hope, when nothing else has succeeded. That is not the case. That keeps people from asking and participating. Trials are available across the cancer journey.

People generally have poor awareness of clinical trials, and many don't understand how medicine works. But they should know that we have decided how and when to use every drug over many decades thanks to clinical trials. We don't just say, "Here's a drug that works in the lab. We know it works with a mouse, so here you go, patient." We don't do it that way.

Do you have any particular prostate cancer clinical trials you'd like to highlight?

Rick: I'm in the genitourinary committee, so I know a little about what's going in the prostate portfolio. There's a trial that we're doing that nobody else would do. We're asking if someone who is initially diagnosed with metastatic prostate cancer should receive treatment for their prostate. By metastatic, we mean the cancer is in the prostate and has spread beyond it.

We have similar questions in some of the other cancers. The general school of thought is that unless you respond to treatment, whether it's chemotherapy or radiation in this particular context, we're going to give you chemotherapy or radiation, but we're not going to give you any other treatment to either surgically remove or radiate your prostate. That's the standard, but there's no good data underlying that.

We're doing a randomized trial, so the computer decides which treatment you get. One group of metastatic patients will get some kind of systemic therapy, whether it's chemotherapy, radiation, or another treatment. The other group will have the surgery or the radiation in addition to the systemic treatment.

How big is the metastatic trial?

Rick: It's a large Phase III trial with more than 800 patients.

[You can review this trial here: https://clinicaltrials.gov/ct2/show/NCT03678025.]

This trial demonstrates SWOG's willingness to research these interesting, needy kinds of questions that nobody else would take on.

SWOG has other counterparts, so this is not just a characteristic of SWOG. This is what the NCI-funded NCTN network groups do.

Is there anything else that patients should know about clinical trials?

Rick: Patients should ask. That's the big thing patients should do: ask questions, and ask for clinical trials. If there is a clinical trial that you think you qualify for, you should consider it, and ask questions about it. You don't have to participate, but ask and consider. You owe it to yourself to do that. And if not, you owe it to those who follow you. It's meaningful work. It may help you, but you shouldn't just do it because you think it's going to help you—we don't know if it will. There is no guarantee, but: ask and consider. Pp

Jake Vinson
Clinical trials + PCCTC

Mr. Jake Vinson is the CEO of the Prostate Cancer Clinical Trials Consortium (PCCTC), a multicenter clinical research organization that specializes in trailblazing prostate cancer research.

Prostatepedia spoke with him about clinical trials for prostate cancer and the pioneering work of PCCTC.

How did you get involved with clinical research administration and patient advocacy?

Mr. Jake Vinson: My involvement in clinical research dates back to college years. My part-time job was working in a clinical research organization, and I really enjoyed that environment and the work that was a being done. I progressed through college and graduate school and subsequently was able to run a number of clinical research organizations. That process brought me to New York about ten years ago to be involved in the Prostate Cancer Clinical Trials Consortium.

As far as patient advocacy, I've grown to distinguish two threads of advocacy, one being patient advocacy and the other being research advocacy. My path in working through drug development and clinical trials has really been geared more toward research advocacy than patient advocacy.

Patient advocacy considers needs at the individual patient level —ensuring they're getting to the right appointments and having the right tests and seeing the right experts. Research advocacy makes certain research is funded appropriately. It ensures that research is being watched over in the right way and that it intersects with the patient advocate component. It's an interesting distinction, but one that I think is important.

What has kept you engaged over the years?

Mr. Vinson: I've always found the organizations that I've worked with and have run sit in a very interesting and unique spot in the continuum of cancer research in that they connect academic investigators who are the subject matter experts; they think about new ways to develop drugs and treat patients; and they connect them with the pharmaceutical and biotech companies who are developing drugs aligned with the scientific programs of investigators. And finally, there is the part that we talked about—the advocacy component. Making sure that patients at the clinical sites where they're being cared for have access to these research studies.

What's kept me involved is being in the middle of that triangle. Not necessarily working in a hospital or in an academic research center. Not necessarily working in a pharmaceutical company. And not necessarily working at a clinic site or a doctor's office, but really creating an infrastructure that connects all of those things. That to me has been exciting.

What is the Prostate Cancer Clinical Trials Consortium?

Mr. Vinson: The Prostate Cancer Clinical Trials Consortium (PCCTC) is an organization that has been around for going on 20 years now. It was originally created by the Prostate Cancer Foundation (PCF), which is the world's most significant philanthropic prostate cancer research-focused organization. They recognized that there were obstacles in the collaboration of what were considered the top prostate cancer academic programs around the United States. They worked to put some funding in each of those centers with the sole goal to eliminate barriers to working together on clinical trials. This was some time ago.

That idea was subsequently leveraged into an initiative through the Department of Defense [DoD], which here in the United States has the Congressionally Directed Medical Research Program. Within that program is the DoD Prostate Cancer Research Program (PCRP).

Fifteen or so years ago, the PCRP put in place an offering for a Clinical Consortium Award. This was a formalizing effort to PCF's idea. Memorial Sloan Kettering Cancer Center (MSK) applied for and became the coordinating center for this Consortium Award. Eight other centers were selected as participating sites. This created the coordinating center site model, or a consortium, to bring together and understand what clinical trials everyone was working on, where the intersects were, and where the collaborations across sites could happen efficiently and effectively. The aim was to shape and understand the landscape of prostate cancer drug development to take out those preconceived notions of competition and show areas where cooperation could happen.

MSK still holds that Clinical Consortium Award. We've had a number of sites come in and out over the last fifteen years.

A number of years ago we identified that to really be effective and to scale our infrastructure to support all kinds of prostate cancer research we needed to have a better business-operating model than something based solely on a grant from the from the DoD.

So, just over five years ago we spun off a business, which is now the operating company for the PCCTC. That business exists to conduct multicenter clinical trials so that all of our participating sites around the world now can work together on selected clinical trials. We let the investigators do what they do best, which is develop the ideas and ways to study the drugs. We let the clinical research sites and the clinics do what they do best, which is treat their patients and manage them on a study. This in turn lets us handle the regulatory, data, and biospecimen management—all of the things that go on behind the scenes of a clinical trial that investigators and sites aren't specifically suited to address. Through contracts with our pharmaceutical partners we are able to get access to their drugs that are developed by the pharmaceutical companies and then put those into the clinical trials that our investigators are developing. That is how our model works.

That's a unique model, isn't it?

Mr. Vinson: It is fairly unique. It has attributes from a number of different businesses in this space. It in and of itself functions in a fairly unique way.

What kinds of clinical trials do you run?

Mr. Vinson: The organization was originally established as an early phase drug development group, so our intention is to identify new drugs, new classes of drugs, or new targeted drugs to treat prostate cancer patients of all stages. We do very early studies with patients who are newly diagnosed or often times we do studies with very late stage patients who maybe have seen a number of lines of treatment already. We really look at the continuum of disease states from very early diagnosis to very advanced disease. We identify which studies would be most reasonable to put in place in all of those spaces so that we're not necessarily constantly overlapping. We want to have studies distributed fairly evenly so that patients of all different disease states or manifestations within states would have an opportunity to be in a clinical trial if treated at one of our sites.

We have traditionally focused in Phase I and Phase II development. Because we've been fairly successful in that, we have now opened our first Phase III study, which is a much larger trial. A Phase I or a Phase II trial has from 30 to 100 patients. A Phase III study can have as many as 800 to 1000 patients.

I've heard that it's difficult to enroll patients in trials and that frequently trials don't get the number of patients they were originally seeking. Why do you think this is?

Mr. Vinson: There is data that shows this is absolutely true. What we know is that, in the United States, 3 to 5 percent of cancer patients go on to clinical trials, which is obviously not very many. Even within the number of eligible patients, only 25 percent actually do enroll in a clinical study.

I should also add that because of the way the science has taken us, we are now looking to enroll patients with specific molecular characteristics. These molecular characteristics are biomarkers, or gene signatures that we see in tumor tissues or blood, which can often be found only in a very small percentage of patients. A particular marker that we think a drug works

in may only appear in 10 or 15 percent of patients. A fairly small group of patients go onto studies to begin with; molecular inclusion criteria makes this number smaller.

This is creating a conundrum whereby we have to cast a much wider net, meaning we have to have more sites collaborating to identify patients eligible for enrollment based on their unique molecular characteristics. These are interesting challenges. The science to be able to do this is incredibly significant and will be impactful to patients, but filling those clinical trials is difficult. We would think we would want to include more patients in studies, but because we'll be able to parse the patients into much smaller groups with specific molecular characteristics, it is becoming more challenging.

You need to cast an even wider net to find these patients?

Mr. Vinson: That's exactly right. We originally worked with eight centers. We now have 14 centers that are formally part of our group with another 50 sites in the United States who are affiliate participants. Those centers have gone through our qualification process; we know they have quality research programs at their clinical sites and have the opportunity to open studies that we're developing as well. That is one of our strategies, to circumvent that conundrum of great science that then doesn't enroll the patients we planned.

There are some regulatory implications here: there has to be great caution in doing clinical research. We would offer that, when you're using drugs in a very early development space, meaning this is often the first time that the drug has been used in patients, you want to make sure that the patients are appropriate to be treated with those drugs. What you can't do is just flood your study with patients because you might miss a safety signal, or you might miss a dosing change. There are too many variables happening at the same time. We know that is part of the issue.

From the other end, it's a lot of work for the clinical sites to participate in the studies. We do our best to fund our sites appropriately, but there are so many pressures on our clinicians in terms of how they're managing their electronic medical records and how many patients are expected to be seen by their clinics and their sites. Their additional bandwidth to enroll patients under clinical trials is finite. You have to consider all of the safety and regulatory requirements for the studies themselves and the external factors for the investigators working on the studies.

Finally, we and others have been working for a long time on research and patient advocacy.

When a patient comes in and they're approached about a clinical trial, we don't want that to be the first time they've ever heard about clinical research. That's an entire other discussion that requires a full education to make folks comfortable with clinical trials. Those are the three angles that we try to work on in alleviating those barriers.

Why should patients consider joining a trial? What are some of the benefits?

Mr. Vinson: Depending on the study, the potential for benefit can vary. There are potential advantages to getting access to a new drug, which could in theory have great

benefit to them, but again, this is called research. We don't know exactly what the outcome will be, but there is the opportunity to get access to more cutting-edge treatment that could have an upside.

The other lens to think about is that research is advancing the field for the men who will follow. If we didn't have the clinical trials that we did 25 years ago, we wouldn't have the drugs that are now proven to extend life . There were men who joined clinical trials to get those drugs approved and tested as safe and efficacious or that worked in controlling cancer. We would offer that there's great opportunity to, in a safe way, contribute to the advancement of treatments for future generations of men. We think that's important.

Is there a certain time point when a man should start looking for clinical trials?

Mr. Vinson: Ideally patients should learn about the clinical research process at the point of diagnosis so they understand the advantages and risks of trial participation. Men should feel comfortable asking their healthcare providers about clinical research opportunities at any point in their care.

From a drug development perspective we traditionally evaluate therapies earlier in the disease continuum only after establishing efficacy in more advanced disease. We think there is potential for a cure in very early disease and are now designing trials of drugs that gave benefit in very advanced disease in this space. We really feel like there needs to be clinical research participation from very early on while we continue to look to control disease that has spread and become more advanced. In short, there are opportunities to participate in clinical trials starting at all points of care.

I suppose if you start a conversation early on with your doctor, even if there's nothing appropriate for you at that time, if something does come up, she is more likely to bring it to your attention.

Mr. Vinson: Absolutely. Opportunities are continually turning over: new studies are opening and prior studies are closing. We know patients from all over the country who have been on multiple clinical trials. Many do very well. We think it's exciting that they're open to that.

Do you have any suggestions that you think patients should keep in mind as they evaluate trials?

Mr. Vinson: There are so many different types of studies out there. I think a Phase I study may have requirements in it for some additional testing or additional visits because the endpoints of that kind of study are to evaluate at very specific timepoints how a drug is being received and metabolized or processed by a patient.

The bigger and later stage Phase II or Phase III studies are designed to be as continuous with standard of care as possible so that it is not a burden or inconvenience to the patient. All of those things have to be taken into consideration. An honest discussion with your healthcare provider, healthcare team, and the research coordinator or research nurses, is really the best way to figure out which situation is going to be best.

How the results of your trials are reported? Are all trials reported?

Are patients who participate in trials informed of the results?

Mr. Vinson: We publish and present all the results from our research studies. We ensure that we have the right to do that with our partners —our research sites and our pharmaceutical and biotechnology partners as well as the groups that own the drugs that we work on. We have contracts with them that are very clear in that we have the ability to put the data together, to put the outcomes together, and present them to the public. That's done through a number of different methods—meetings where abstracts are presented to manuscripts submitted to professional journals.

Your point is a good one about returning results to patients. Many sites have programs to distribute the outcomes to those patients. This is done at the site level. The challenge for us is that we don't get, in almost all cases, direct contact information for patients. When a patient goes on a trial, the local treating clinicians certainly know that patient well. But we give that patient what we call a *subject identifier*. This is a random number that is created so that we can then track that patient without having any personal information about the patient directly. We have their health outcomes data, but we certainly don't know where they live, or what their phone number is, or how to email them. Returning those results directly to a patient from the entire study as you can imagine, is something that would be challenging.

Informed consent forms reflect the growing number of molecular testing and sequencing performed in trials. Before patients participate on a trial they are clearly notified on of which test results would be returned to them personally. This can vary from study to study.

But to your point, we think it's important when we're doing research tests that could have implications for a patient or their families, especially when we're talking about genetic testing, that we have a mechanism to inform them if there are findings that need to be followed up. As you can imagine, there are implications for family members as well in genetic research. That happens through the informed consent process, and again, at the site level where the patient's being treated.

I guess if you're going to make a call for men to join trials for altruism's sake and for the furtherment of science, they might want to know if the research actually did advance our understanding of prostate cancer.

Mr. Vinson: There are sites that do that: when outcomes are published, they distribute them to patients who are interested. In addition, publications can be searched for independently or requested from the clinical investigator.

It takes a long time for some of these studies, though. If you're the first man to go into a particular study and it's going to be a 100-patient trial that takes over a year, you're already taking about 18 months to enroll that study. Then we do all the follow up, which could be another two years. Then we do all of the data analysis, which could be another six months. It could be three to five years from the original patient enrolled to publication. It can certainly be a long process.

Are any particular PCCTC trials looking for patients that you'd like to highlight for my readers?

Mr. Vinson: We're doing a study called IRONMAN (https://ironmanregistry.org/patients/). IRONMAN is an international registry for men with advanced prostate cancer. We're working with eleven countries around the world in collaboration with the Movember Foundation. (Movember is the Australian-based organization that grows mustaches and raises money every November for men's health and awareness.) One of their core programs is a prostate cancer program, and one of their key projects is the IRONMAN project.

The PCCTC is the global coordinating center for IRONMAN. The study does not have a specific drug treatment requirement and instead tracks patients receiving standard of care therapy. Participants will be recruited across academic and community practices from around the world to facilitate a better understanding of variations in prostate cancer treatment. Patients who enroll are followed prospectively over several years. We collect data on what treatments their physicians have given them as well as some high-level clinical outcomes data from those treatments and track how treatments are sequenced or given in combination around the world.

The second part of the trial examines patient reported outcomes. We have particular surveys that study participants complete every three months that examine their quality of life and how they're feeling across a number of domains. Then thirdly, we have a biology component, in which we collect blood samples when patients join the study and then again each time they change their treatment. This helps us understand, to the point I was making earlier, what changes are happening at the molecular level and what's changing in the biology of the patient. Then finally, we're asking their physicians to answer a brief survey telling us why they recommended changes in treatment, which will give us insight into the variations in prostate cancer treatment across different centers and countries. By collecting blood samples, patient reported outcomes, clinical data, and physician surveys, we can tie together the biology of the patient's disease with the patient's reported experience on a given treatment with the clinical data on their response to treatment. Putting all of those things together with 5,000 men around the world in eleven countries is going to give us an incredibly rich dataset to be able to mine and understand what treatment patterns may be best for particular patients. What's unique about IRONMAN is that we are not just collecting information on how patients do clinically, but also how the patients themselves report they do. Through IRONMAN, we will also understand the biology of those patients and how it changes over time, and we will be able to tie those outcomes to the clinical outcomes to develop tests that can potentially let us predict how patients will do on a specific treatment.

IRONMAN is an exciting study. Centers around the world are now open and actively participating in the study. We have nearly 700 patients accrued from 7 countries, with 4 more coming on board soon. It's an exciting project, and something that is very different than a standard Phase I or Phase II clinical trial, but it's certainly something that we think is going to result in an incredibly powerful dataset for investigators to use into the future. Pp[1]

Merith Basey
Reporting Clinical Trial Results

Ms. Merith Basey is the Executive Director of Universities Allied For Essential Medicines (UAEM) North America, a global network of university students who believe that their universities have an opportunity and a responsibility to improve access to publicly funded medicine developed on their campuses.

Prostatepedia spoke to her about UAEM's transparency campaign to get universities to report the results of the clinical trials they run and how prostate cancer patients can help.

How did you get involved with health advocacy?

Ms. Merith Basey: A little bit by accident. My interest in public health and health advocacy stemmed from my undergraduate degree in modern languages and my interest in Latin America.

In 2004, I volunteered with an organization in Ecuador called AYUDA in conjunction with a local diabetes foundation that worked with children with Type 1 diabetes and their families. We worked together to provide diabetes education to children with Type 1 and their families so that they could learn how to better manage their condition and increase access to resources.

It changed my life. I ended up working for that organization for a number of years in a number of different settings. However, during that time, I began to see that, in some of the countries in which we worked, access to insulin was an ongoing challenge, and for many families, the price of insulin was simply too high. The lack of action at that time spurred me and a small group of advocates to launch the 100 Campaign for access to insulin back in 2012. Today, one in two people who need access to insulin still don't have regular access, a challenge that is increasingly apparent in the United States and in many countries around the world. It was through this lens that I ended up in health advocacy.

What is Universities Allied for Essential Medicine?

Ms. Basey: Universities Allied for Essential Medicine (UAEM) was founded in 2001 at the height of the HIV/AIDS epidemic. A drug called d4T, or stavudine, had been developed at Yale University with public funds and was being used as part of a cocktail of drugs, at least in the United States, to treat people living with HIV.

At the time, Doctors Without Borders/Medecins sans Frontiers (MSF) was looking to treat people living with HIV in South Africa where the burden of disease was highest. They realized that the price of this one drug was too high for them to be able to treat the millions who were in need of access to treatment. However, a young student and activist who started Yale law school that year decided to take action. She organized, with other students in conjunction with MSF and Civil Society, with the goal of lobbying her university and the company Bristol-Myers Squibb (who had purchased the rights to the drug) to change the license between them to allow for the legal generic importation of this drug into South Africa. The campaign was a success; it led to a 90 percent reduction in the price of that drug in that region, allowing MSF to treat people living with HIV for the first time.

That's the founding story of UAEM and is at the heart of our work, primarily based on university campuses in the United States and today in over 20 countries around the globe. A simplified vision of our work is that we believe no one should be poor because they're sick or be sick because they're poor. We understand the role that universities have in the drug development pipeline and believe that they should be critical partners and leaders in ensuring access to affordable medicine, especially when it is developed with taxpayer funds. Also, in particular, we work to urge universities to increase their research into neglected diseases since most research in the current system tends to go into drugs or treatments for wealthier and historically whiter populations. A lot of other drugs for diseases that predominantly impact the poor are left behind until there's an urgent demand like there was for Zika and Ebola. It is estimated that 90 percent of the research dollars go to just 10 percent of the global burden of disease.

Do you focus on universities because that is where some of this initial research is done or because you're trying to activate younger students on campus?

Ms. Basey: I think it's both in part. Initially, it was inspired by that success story at Yale, but it was also about understanding where students have power. Students are key stakeholders in university systems, and while they are actively enrolled, they have unique power and access to faculty and other decision-makers. They have the right to be able to meet with the administration, ask them about their policies, and urge them to address historic inequities or errors.

Secondly, universities are the key drivers of much of our most innovative biomedical research. In the United States, for example, every year $37 billion of taxpayer money goes in the form of grants from the National Institutes of Health (NIH) to universities across every state and in a number of countries around the world to do biomedical research and clinical trials.

Given this massive public investment into researching and developing new compounds and medical innovations, it is also an opportunity to influence the way that those drugs are patented and eventually licensed into the hands of pharmaceutical corporations down the line. We also believe that the public should have a return on that investment and that the product of that investment should be accessible and affordable to the people who paid for them in the first place: the public.

Yes, the National Cancer Institute (NCI) and the National Institute of Health (NIH) fund quite a number of clinical trials. Most of the people reading this are familiar with trials as potential participants. But what happens when a trial is completed?

Ms. Basey: It depends on who is leading the trial. In the United States, for example, when a university is responsible for leading a clinical trial and it is completed, the results should be reported onto a public database within a period of 12 months. (There are of course exceptions based on a number of different criteria). A significant portion of NIH funding is invested into clinical trials. It's estimated that in 2017, at least about 38 percent of that $37 billion figure that goes to universities actually goes directly into funding for university-driven clinical trials, clinical research, and other activities related to clinical trials.

On average, however, it has been estimated that only about 50 percent of clinical trials are registered and reported. This obviously has impact. I can't speak for the specific motivations that certain individuals might have for entering a trial, but in general, people participate to help find out more about the effects of specific treatments on a particular disease whether that be in the hope of helping improve their own health or the health of others. Knowing that, it's unethical that this data goes unpublished.

Why is this data not reported?

Ms. Basey: A couple of things are happening. Obviously, that 50 percent is a global figure so it is a global problem. In the United States, however, even though the FDA Amendments Act makes it required by law for certain trials to be posted, according to UAEM's recent report (www.altreroute.com/clinialtrials) 31 percent of trials that are due are *still* missing results on the public registry with performance varying strongly between the top 40 institutions reviewed.

Why are they not reporting? In some cases, they don't report because they haven't been required to, because it takes time, and because often the results are not favorable to the people funding the trials. Trials with negative results are two times as likely to go unreported as trials with more positive results. Publications typically like to report favorable outcomes rather than negative outcomes. If you are a private pharmaceutical corporation funding a trial for a drug you intend to produce and the initial results are not in your favor (due to limited effects on health outcomes or number of adverse effects) or if there isn't a legal obligation to report, you may choose not to publish data. Obviously, this is entirely unethical but the evidence suggests it happens.

Best practices are set out to say that all clinical trials should be posted because, without all the data it's going to skew data in a manner that is ultimately harmful. It's going to skew the results. It's going to skew the information that doctors are going to have in terms of deciding which drug is safer than another. The system is flawed in that sense. Failing to publish trial results means the decisions-makers with regards to medical treatments won't have full information about the benefits or risks of treatments.

Just to clarify for patients, how are the results of clinical trials usually reported?

Ms. Basey: In the United States, a trial would first have to register on clinicaltrials.gov when the trial starts. (Although not all studies are required to be registered, e.g. observational studies or trials that do not study a drug, biologic, or device). Clinicaltrials.gov is a United States government database that has all that information for both federally and privately funded trials conducted under investigational new drug applications to test effectiveness of experimental drugs for serious or life-threatening diseases or conditions. Because of this FDAAA Final Rule, specific trials that involve patients will need to register or report their data within 12 months on that same database.

At UAEM, in conjunction with TranspariMED, we just looked at the top 40 United States universities driving a lot of this biomedical innovation via clinical trials. Even though the law required that they register and report data within 12 months, about a third of these university-driven trials were unreported.

Essentially, they're breaking the law. For every day that they hadn't reported, the FDA could fine them $10,000. There's quite a large incentive (beyond the ethical one) for them to report, but the FDA so far hasn't collected any fees.

We need to be making sure that all data and all trials are ultimately registered and reported so that there is full transparency and full information for everybody in terms of open data. It really comes down to making sure that data isn't hidden.

So you're running an awareness campaign?

Ms. Basey: For us, it's very clear that, as receivers of public funds and given their social missions, universities should be leading the way in terms of registering and reporting of their own clinical trials.

The campaign that we're running is not only to urge universities to register and report but to go a step further. The World Health Organization (WHO) developed a joint statement on public disclosure of results from clinical trials. This was first signed in May 2017 by 21 key funders of clinical trials around the world including the Wellcome Trust, the Gates Foundation, MSF, the Indian Council of Medical Research and the Drugs for Neglected Diseases Initiative, just to name a few. They agreed, that if they fund clinical trials they will require investigators to register and publicly report the results in a timely manner.

We go little bit further because we are also asking those universities or institutions to come up with a policy to hold themselves and others accountable. We have students in over 50 universities in North America and in 20 different countries around the world organizing on their campuses to urge their universities to make sure that they're registering and reporting their own clinical trials and thinking about signing this WHO joint statement on clinical trial transparency.

Is there anything that my readers can do to help?

Ms. Basey: If you've had the privilege of going to a university, call or email your alma mater to ask them about their policy or their performance if they are listed in our report. Let them know that this is something you support and you'd like them to take action. We know that universities respond to pressure from their alumni.

You could also financially support UAEM's grassroots campaign directly via www.UAEM.org.

At UAEM we will continue to urge universities to step up to their commitments. They are, ultimately, morally bound to be transparent with their research outcomes since most of these trials are publically funded. We're really proud to see that the universities that are 100 percent reporting are actually beginning to mobilize and think about moving forward with signing onto the WHO statement. But we still have a long way to go. Every pressure and encouragement is recommended.

Clinical trial transparency helps accelerate medical progress for new treatments and improve our understanding of treatment efficiency and safety, ultimately contributing to improved access to medicines and better health outcomes for us all. Pp

Helping Patients Navigate the World of Clinical Trials

Ms. Merel Grey Nissenberg, a California attorney specializing in medical malpractice cases, is the President of both the American-based National Alliance of State Prostate Cancer Coalitions and the California Prostate Cancer Coalition.

Mr. Tom Kirk is the Vice-President of the California Prostate Cancer Coalition and an Invited Guest of the Executive Committee of the National Alliance of State Prostate Cancer Coalitions.

Together they form Informed Health Consulting, a group that helps patients of all kinds find clinical trials appropriate for them.

Prostatepedia spoke with them about how, why, and when patients should consider a clinical trial.

How did each of you become involved in prostate cancer advocacy?

Ms. Merel Grey Nissenberg: In one of the cancer cases I was handling in my medical malpractice law practice, the surgical oncologist recommended that I join the Prostate Cancer Task Force for the California Division of American Cancer Society (ACS). I ended up co-chairing the group the next year. I have also handled a lot of medical malpractice cases involving prostate cancer, among other cancers—especially inexcusably late diagnoses of prostate cancer. I became an advocate for patients in that way as well.

In 1997, ACS, California Division held a statewide meeting on prostate cancer. During the conference a few of us suggested that California should have its own prostate cancer coalition. People thought it couldn't be done because the state was so big. We're now in our 22nd year!

Along the way, we started the National Alliance of State Prostate Cancer Coalitions in 2004 (www.naspcc.org) to serve as an umbrella entity over the existing and future state prostate cancer organizations around the country.

Mr. Tom Kirk: I got involved in prostate cancer in 2004 when I was recruited to be the President and CEO of Us TOO (https://www.ustoo.org/.)

That was about the same time that the National Alliance of State Prostate Cancer Coalitions was formed, so I have known Merel and her work for many years

When I started at Us TOO, one of the strategic plan goals was to increase the amount of educational materials by 100%. For many years, educational material development remained the focus of Us TOO. Of course, we also focused on support groups and support group leader training.

I left Us TOO in 2016 and moved to California where I quickly started work with Merel and the California Prostate Cancer Coalition. I've been the Vice-President of the California Prostate Cancer Coalition for a number of years. I also became involved in the National Alliance of State Prostate Cancer Coalitions as Invited Guest of the Executive Committee, and Chair of its Steering Committee.

Before Us TOO, I was on staff at the National Alzheimer's Association and had an interest in advocacy.

What is Informed Health Consulting?

Ms. Nissenberg: Informed Health Consulting is our consulting group. Tom and I concentrate in three areas: we set up Patient Ambassador programs; we set up Patient and KOL Roundtables; and most importantly, we do Patient Accrual for Clinical Trials using a direct patient model.

Informed Health Consulting (IHC) has a very unique methodology. Unlike clinical trial matching services, we work directly with the patients. We know the patients. We're involved in advocacy groups. We are embedded in and between advocacy groups.

IHC does all of its activities across different types of cancer and different disease sites.

For example, we were working for Medivation, which has since been purchased by Pfizer, on a trial that looked for women with advanced or metastatic breast cancer who had a BRCA 1 or BRCA 2 mutation. When we first talked to the company, they said, "We cannot get the last 100 patients. We have tried and tried."

Tom and I identified which patients we needed to approach. We were pretty imaginative, which is what we do. We came up with great ways to meet patients who would be really good candidates for the trial. We went to national and local breast cancer advocacy meetings. Since BRCA 1 and 2 mutations are very frequently seen in Jewish populations, we targeted Jewish university women and big Synagogues on the West Coast.

Long story short, we helped accrue the rest of the patients, the trial closed, and it was a positive trial. The drug, a PARP inhibitor, has already been approved.

It's so exciting because we can really see the fruits of our labors. Hopefully, we have helped to save lives.

You had a direct impact.

Ms. Nissenberg: IHC is unlike a clinical trial matching service that doesn't really get to know the patient until the patient or their physician contacts them. Companies don't have that personal relationship. Tom and I start out with the personal relationship.

It's been really successful. We hope that we're helping to accrue patients who can benefit from an appropriate trial.

What might some of the benefit be? Why should patients consider a clinical trial?

Mr. Kirk: Often a clinical trial is the best way to gain some access to new developing interventions.

Ms. Nissenberg: First of all, the control group is always going to receive at the very least, standard of care. It's not like you're not going to get care that hasn't already been approved or in practice. But it is an opportunity to see if there is a new therapy or intervention that can benefit patients.

If the response is really striking, they'll stop the trial midway through after the interim analysis and let patients cross over into the group that is showing great success.

A trial is an opportunity to take advantage of new therapies and new interventions that may ultimately become standard of care.

Mr. Kirk: The word you just used, interventions, is essential. Often, clinical trials develop new approaches to treating patients. It's not just access to a drug per se, but also about access to the latest care.

Frequently at a reduced cost, right? Sometimes trials cover the cost of the drug or procedure.
Ms. Nissenberg: Absolutely.

Some of the numbers people bandy about for clinical trials are not quite accurate. In an issue of the The National Cancer Institute journal that just came out this year, a study shows that the barriers to entering clinical trials are structural, cultural, or clinical for more than three-quarters of cancer patients.

Everyone says that generally 8 percent of patients enter a trial, but only 3 percent of cancer patients. However, this study says that that number is too low.

They performed a meta-analysis. Nearly 56 percent of patients did not have a trial available to them at their institution. Nearly 22 percent were deemed ineligible. [That's what they mean when they talk about structural and clinical barriers.] That low number of 2 - 3 percent is from the 1990s and early 2000s. It was largely based on enrollment in government-sponsored trials. About twice as many patients are enrolled in pharmaceutical-sponsored trials.

The authors of the NCI article believe that an estimate of 8% is likely more reflective of patient involvement in cancer clinical trials, government- or pharmaceutical-sponsored.

Still, 8% is pretty low when you think about it.

Ms. Nissenberg: Absolutely. However, the authors made an important observation: when patients are offered an available clinical trial, they choose to participate only about 50% of the time. That's shocking. I didn't realize it was that high.

Why the reluctance in the other 50 percent?

Ms. Nissenberg: I used to be in something called the Summit On

Cancer Clinical Trials. I was part of the dissemination strategy to create a piece for the NCI website to help patients learn what clinical trials are, long before they ever need or consider joining one.

The term clinical trial itself is very foreboding. A lot of people think either of guinea pigs or they think of the boy in Pittsburgh who died after being inappropriately consented for the trial. Or they picture a green-tiled room with a big light hanging down: very stark, very cold. They feel that it's experimental. I think people worry about that. I think that's why they primarily don't join.

I think a lot of patients think of the clinical trial as a last resort. When your cancer has become so advanced that you're willing to try something experimental. That's not true obviously. Given that, at what stage along the prostate cancer journey should a man consider a clinical trial?

Mr. Kirk: Don't we always say that men should be active in their treatment? We encourage men to be very active, to be the quarterback or CEO of their own care. That would mean he should look for a trial at any stage.

Of course, we would believe the earlier stage is important because men are starting to make decisions about whether to treat or not. Approaches like active surveillance often are developed in clinical trials.

At any stage, it's important for people to explore their clinical trial options. Search early and often.

Are there many prostate cancer clinical trials available for the newly diagnosed?

Ms. Nissenberg: Just a few. Most of the trials are for advanced prostate cancer. But as you know, advanced prostate cancer can be non-metastatic. There have been important clinical trials in this space as well. If we can delay, or maybe prevent metastases altogether, then we're going to go a long way to improving overall survival.

Do you think it's in a man's best interest to keep abreast of what kinds of clinical trials are available, even if they're not necessarily for his current disease state?

Ms. Nissenberg: That's easier said than done. There are a lot of trials out there. IHC has done a project with a group called Emerging Med. We are helping all prostate cancer groups place a clinical trial finder on their websites. These clinical trial matching finders have computer algorithms that match trials to patients.

What should a man reading this who is interested in finding a trial do?

Ms. Nissenberg: The first thing is to go to www.clinicaltrials.gov. That site lists all the NCI-approved cancer clinical trials. It doesn't list all the trials out there, but it lists most of them.

A lot of physicians either don't know about all the applicable trials or they don't really want to send their patient away to a clinical trial unless they're going to get the protocol and do it themselves.

Why?

Ms. Nissenberg: Some are disincentivized because they're going to lose a patient or lose money. That's just reality. And patients don't always qualify. Sometimes patients will come armed with information about certain trials and the physician hasn't heard of any of them. Then, the patient could contact a company like Emerging Med and say, "This is my status. Is there a trial that you would recommend?"

Mr. Kirk: The National Alliance of State Prostate Cancer Coalitions will be offering this service on our website. We believe these matching services are important. The case management services and individual discussions with a case manager can be very helpful in removing the stress of finding the right kind of clinical trial.

Ms. Nissenberg: This is in contrast to other sites that only have a couple of sponsors' trials. They're not getting all the trials out there. They're only getting the ones that those sponsors are enrolling and that don't necessarily apply to that patient or his condition. You have to be really careful that you're looking at a completely objective, non-commercial source for clinical trial listing.

A man can look for trials from a variety of sources: online, through his doctor, through one of these clinical trial matching services and then come up with a short list of trials that he may be interested in?

Mr. Kirk: Yes.

Are there any other considerations men should keep in mind as they evaluate appropriate trials?

Ms. Nissenberg: Be realistic. See if a trial is geographically appropriate or determine if your own physician can run the protocol. Look at quality of life issues—are there known side effects that you're not going to want to deal with? But then look at the positive side too. The control arm should never be less than standard-of-care treatment. But keep in mind that if it is truly a randomized control trial, which is the kind that we really need to set new standards of care, you're not going to be able to choose the arm of treatment. You have to be willing to go into the trial knowing that you could just get standard of care and not the new therapy or intervention. The trials are blinded; you don't know what you're getting.

Isn't it true that even men on the control group tend to do better because they're being monitored more closely?

Ms. Nissenberg: That's true. They have much better care. They've usually got an oncology nurse assigned to them. Sometimes those getting standard of care or placebo end up getting some of the benefits, especially the psychological benefits, because they think they're being treated with the new treatment. The placebo effect is very interesting.

The placebo effect can be positive.

Mr. Kirk: Right.

Any final thoughts for men as they start to look for clinical trials or consider clinical trials, any final advice?

Mr. Kirk: Remain active. Know that your contribution is about more than just yourself. Share with others your experience of being in a clinical trial to help other men deal with their hesitancy.

One way might be to join IHC's Patient Ambassador Program. Can you talk a bit about that program?

Ms. Nissenberg: We develop groups of Patient Ambassadors. Let's say a company has a genomic test, for example. We identify a group of diverse patients—diverse in terms of geography, socioeconomics, and race. We bring together about 15 or 16 men who have had this genomic test and want to share their experiences with other men. We bring them in for a weekend. We bring them to the company. They have a tour of the facilities. They meet everybody. They completely bond. We train them on how to go out to support groups and to civic groups like Rotary Club to talk about the test and what it meant to them.

We then maintain a call list. If a patient wants to talk to another patient who has had this test, we set up a phone call. We've had patients go to other states to talk about whatever the product is. (It could be a therapy or a test.)

Mr. Kirk: This is personal advocacy based on experience.

You mentioned genomics as one grouping but how many of these patient ambassador groups do you have?

Ms. Nissenberg: It depends. We have to be careful because we're not marketing anything for anybody. These Patient Ambassadors aren't marketing people and we're not selling a product. We're just sharing patient experiences.

Another thing Informed Health Consulting is doing are Patient Roundtables. For example, in October of last year, we had a Roundtable on bone health and access to bone-targeted therapy. Access to care is a hot-button topic.

Mr. Kirk: For not only prostate cancer, but also for breast cancer.

Ms. Nissenberg: Right. We brought in prostate, breast cancer and lung cancer patients. These were people who were dealing with bone mets, osteoporosis, or osteopenia. We brought in physicians to talk to them and to help them with access issues.

We're going to be doing another Roundtable on step-therapy in the Fall.

The Roundtables are great because we can bring people in from anywhere in the country. We teach them. We can find out from them what they're hearing in their local communities. For example, if there is an access issue, what are they hearing? Where is their pushback? It could be on a therapy. It could be on access to different tests. It could be coverage issues.

You mentioned that these patient roundtables are not prostate cancer-specific. Is the Patient Ambassador Program also not prostate cancer-specific?

Ms. Nissenberg: Correct. We develop Patient Ambassador groups for any disease. It's the same modality. The most time-consuming and challenging parts are not the planning for the meetings or trainings. The hardest part is identifying the right patients for both programs. Pp1

If you're interested…

…in participating in Informed Health Consulting's Patient Ambassador or Patient Roundtable programs, contact Merel at merel@informedhealthconsulting.com or Tom at tom@informedhealthconsulting.com.

Both can also be reached by calling 424-253-1169.

Mark D. Hurwitz, MD, FASTO, FACRO
NRG Trials

Dr. Mark Hurwitz, a widely recognized leader in the fields of thermal medicine and genitourinary oncology, is the Vice-Chair for Quality, Safety and Performance Excellence and Director of Thermal Oncology for the Department of Radiation Oncology at The Sidney Kimmel Medical College at Thomas Jefferson University in Philadelphia, Pennsylvania.

Dr. Hurwitz talked to *Prostatepedia* about NRG Oncology and a trial he's running with them that looks at anti-androgen therapy and radiation therapy with or without Taxotere (docetaxel) in treating patients with prostate cancer that has been removed by surgery.

Why did you become a doctor?

Dr. Hurwitz: Medicine is an extraordinarily rewarding career in regards to being able to help people at important and often critical junctures in their lives. It's extremely humbling to see strangers walk into my office and put their trust in me to help them through a difficult time in their lives.

It's an enormous responsibility.

Dr. Hurwitz: It is, but one that comes with many years of training and preparation for a physician to get to the point when we enter practice.

What is NRG Oncology? What has been your involvement with the group?

Dr. Hurwitz: Several years ago, the National Cancer Institute (NCI) mandated the merging of cooperative cancer research groups into fewer but larger groups. One of these groups NRG Oncology, was the result of the merging of the Radiation Therapy Oncology Group (RTOG) with the Gynecologic Oncology Group and the National Surgical Adjuvant Breast and Bowel Project (NSABBP). This dynamic new large cooperative research group is primarily supported by the NCI. It's been exciting and rewarding to be a part of this new larger group putting all our resources together to bring trials to patients.

I've been involved with NRG Oncology since its inception. Predating that, I was involved with both RTOG, as well as the Cancer and Leukemia Group B (CALGB) during my years at Harvard Medical School.

What kinds of trials does NRG oncology run?

Dr. Hurwitz: The focus of cooperative groups, including NRG Oncology, is on conduction of clinical trials to answer important questions that are best addressed by getting multiple centers involved. These tend to be Phase II or Phase III trials involving hundreds, and sometimes thousands of patients, to answer a critical question that experts in a given field see as being one of the most impactful issues to address for a given set of patients.

NRG is also involved in translational science as well. Almost all of our clinical trials have an incorporated translational aspect to them to answer leading-edge questions in regards to some of the pertinent science behind advancing treatment for our patients.

Are the participating institutions limited to within the US?

Dr. Hurwitz: There are international participants. The group does have a North American focus. Therefore, the United States, as well as many Canadian institutions, are very active in NRG, but NRG has branched out to include international institutions outside of North America as well.

Is it difficult to enroll patients in trials?

Dr. Hurwitz: We all in academic medicine seek to engage more patients with involvement in clinical trials. Only a small percentage of patients nationally participate in clinical trials, so there's a real opportunity to match patients and their needs with the clinical trials that will help advance the field, as well as their own personal care.

Some of the challenges include having appropriate trials available for patients seen within a practice, as well as the time commitment both in terms of the extra time that the physician needs to take to explain trials as well as the resources needed to support the conduction of clinical trials at a given site.

There is also the issue of awareness both on the patient and provider sides as to opportunities for clinical trial participation.

Why should patients consider joining the clinical trial?

Dr. Hurwitz: There are several reasons for patients to consider trials. A trial often provides patients access to leading-edge therapeutic strategies that may not be available off clinical trials.

It also will help provide additional information that will benefit future patients, although our focus is always on the patient who is sitting in front of us.

Also, interestingly enough, there are multiple studies that have looked at the impact of clinical trial participation on patient outcomes, with very consistent findings that patients on clinical trials tend to have better outcomes including survival outcomes than patients not on clinical trials. This is likely due to a number of factors, including the rigorous monitoring of patients on clinical trials as well the follow up after treatment that is done. These patients are followed very closely. There are state-of-the-art treatment guidelines that must be followed on clinical trials to help reduce undesirable variability in patient care. These aspects of clinical trials help to improve outcomes regardless of the particulars of any clinical trial.

> *"These tend to be Phase II or Phase III trials involving hundreds, and sometimes thousands of patients."*

Are there certain stages along the cancer journey when a patient should consider a trial?

Dr. Hurwitz: There are clinical trials that are suitable for patients across the whole spectrum of disease severity. In the case of prostate cancer, there are trials for patients with very favorable risk disease for which active surveillance is an option to trials for patients who are on second or third line interventions for metastatic prostate cancer. And everything in between. It's not a matter of whether a patient has a certain stage of disease. There are questions to be answered at each stage of a given disease for which clinical trials may provide benefit.

Are there any considerations patients should keep in mind as they evaluate trials?

Dr. Hurwitz: People have to gauge the particulars of a trial much like the particulars of any proposed treatment for malignancy in regards to what makes them most or least comfortable with the options before them.

Let's say a patient participates in an NRG trial. Are they informed of the results once the trial is completed?

Dr. Hurwitz: There have been increased efforts in recent years to disseminate outcomes of trials to patients. It's a particular challenge in some diseases like prostate cancer where the results may come a decade or more after trial participation.

That's true.

Dr. Hurwitz: There is an effort regardless of the outcome of the trial to make not just practitioners but patients aware of the results.

Are there interesting NRG prostate cancer clinical trials that you'd like to highlight?

Dr. Hurwitz: I'm happy to highlight NRG-GU002 (https://clinicaltrials.gov/ct2/show/NCT03070886), for which I am privileged to serve as the principle investigator.

This trial builds on a prior Phase II single-arm RTOG trial, RTOG-0621, which I led that revealed very promising outcomes with the addition of Taxotere (docetaxel) and hormonal therapy to radiation for patients with adverse risk factors post-prostatectomy.

NRG-GU002 builds upon the single-arm Phase II trial as a randomized Phase II into Phase III trial exploring the use of radiation and hormonal therapy with or without Taxotere (docetaxel) in men who fail to achieve a PSA nadir of less than 0.2 nanograms per milliliter after prostatectomy.

This is a particularly high-risk group of patients in regards to risk of subsequent treatment failure. We have been very encouraged

by the efficacy of Taxotere (docetaxel) in treating prostate cancer. Taxotere (docetaxel) has been shown initially in metastatic prostate cancer and subsequently in locally advanced disease to have a survival advantage—as opposed to using radiation or hormonal therapy alone in the primary treatment setting. Therefore, there is a lot of interest in exploring its utility in the post-prostatectomy setting for high-risk patients.

Are you enrolling this trial right now?

Dr. Hurwitz: Yes, the trial is actively enrolling patients. There are also some very interesting correlative science objectives to the study, including looking at how genomic profiling may be able to provide additional prognostic information and, importantly, predictive information about which patients may specifically benefit from use of chemotherapy.

Genomic profiling looks at the gene profile of the tumor. We use tissue from the prostatectomy specimen. This means that no additional procedure is needed for the patient to help provide more specific personalized information about their tumor and, again, how certain treatments like chemotherapy may be directed to certain subsets of patients in the future.

This is incorporated as a key secondary objective of the current trial.

If a patient is interested in participating in this trial, can he contact you directly?

Dr. Hurwitz: I encourage patients to have a conversation with their oncologist or urologist first. Their personal physician can help to identify specific trials that may be appropriate for him. NRG also has a website where patients can get information (see https://www.nrgoncology.org/), and if questions remain, they can certainly reach out to the central office at 267-519-6630 or to me to get additional information.

"Only a small percentage of patients nationally participate in clinical trials."

Are there any specific eligibility criteria you'd like to highlight for GU002?

Dr. Hurwitz: Eligible patients are those who are post-prostatectomy with a Gleason score 7 or greater and a PSA nadir, nadir being the lowest level achieved post-prostatectomy, equal to or greater than 0.2 nanograms per milliliter.

In addition, patients have to have staging that demonstrates no involvement of the lymph nodes or distant metastasis, and surgery has to be within one year of study enrollment.

Apart from this particular trial, I encourage patients to give strong consideration to clinical trials in general. As mentioned before, there has been demonstrated benefit just by participating on a clinical trial. This is the way that we advance our patients' care. Clinical trials play a critical role in improving all types of care across medicine. And for cancer patients, where there is all too often little room for error, getting it right when it comes to best clinical practices is essential. Clinical trials help us achieve this goal. Pp

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Coming Up!

June:
Outreach and Advocacy