Newsletter

Prostate Cancer 101, Inc.

http://prostatecancer101.org

August,2020

The Prostate Cancer Information and Support Group of the Mid-Hudson

The Big Picture for U.S. Cancer Statistics:

Good News Overall, Complicated for Prostate Cancer

©David Taylor

The latest statistics on cancer rates in the U.S. shed light on the path of the disease over the last 29 years. Every year, the American Cancer Society releases new estimates on cancer cases and deaths in the U.S. The report in the journal CA: A Cancer Journal for Clinicians contained some excellent news: the cancer death rate has fallen continuously from 1991 to 2017, with a 29% overall decline. This means that 2.9 million fewer people have died from cancer than if the death rates had remained at their highest prior to this period. In addition, the rate dropped 2.2% from 2016 to 2017, the largest drop ever reported. These reductions stem primarily from long-term declines in death rates for four major cancers: lung, colorectal, prostate, and breast.

However, when looking at recent prostate cancer data, the statistics become more complicated. From 1993 to 2017, the prostate cancer death rate dropped by 52%. However, the report also noted that over the last decade, the prostate cancer death rate has stabilized. In *Cancer Network*, lead author Rebecca L. Siegel, MPH, said, "Improved early detection is needed, especially for prostate cancer. Rapid declines in prostate mortality in previous years have halted, most likely because of rising incidence of metastatic disease diagnoses due to the discontinuation of PSA testing to screen for prostate cancer."

The background

In 2008 and 2012, the U.S. Preventive Services Task Force released recommendations against routine PSA screening, first for men over 70 and then for all men. "This has led to a dangerous hiatus in PSA testing in many men, and a total lack of PSA testing in many others," Dr. Catalona said.

Consequently, from 2007 to 2014, there was a steep decline in the number of prostate cancer cases diagnosed in the U.S.

A rise in metastatic prostate cancer

Another study, published in the journal *Cancer*, looked closely at the recent prostate cancer trends. The report found that from 2010-2015, while fewer men were diagnosed with localized prostate cancer, more men were diagnosed with metastatic disease. Specifically, localized cancer cases decreased from 195.4 to 131.0 per 100,000 men ages 50-74 years; for metastatic prostate cancer, the rates increased from 6.2 to 7.1 per 100,000 men. For men 75 years and older, the incidence per 100,000 men decreased from 189.0 to 123.4 for localized prostate cancer and increased from 16.8 to 22.6 for metastatic disease. "This report illustrates recent prostate cancer 'reverse migration' away from indolent disease and toward more aggressive disease beginning in 2012," the authors wrote.

In 2018, the Task Force revised their recommendations. They now recommend shared decision making regarding PSA screening for men ages 55 to 69 years old. However, they still advise against screening men age 70 and older. Research will contin-

ue to assess whether this has an impact on prostate cancer in the U.S., and QUEST will continue to report on these studies as they are published.

Dr. Catalona's Response

The "dark ages of PSA screening" decade from 2010-2018 has produced an entire generation of primary care physicians and internists who don't believe in PSA testing. Consequently, we are now seeing many more men being diagnosed with advanced prostate cancer. This failure to order PSA testing pursuant to the guidelines will compromise the greater than 50% decrease in prostate cancer mortality that occurred in the U.S., Canada, and other countries to a lesser degree during the PSA screening area from 1991 to 2010.

2020 U.S. Prostate Cancer Statistics and Estimates

Prostate cancer remains the second leading cause of cancer death in U.S. men; only lung cancer is more deadly. The American Cancer Society estimates that in 2020, 191,930 men will be diagnosed with prostate cancer, and 33,330 men will die from the disease. About 1 man in 9 will be diagnosed with prostate cancer during his lifetime.

Yet, the five-year relative survival rate for prostate cancer is currently high at 98% for all stages of prostate cancer combined. However, the survival rate for men diagnosed with distant stage disease, in which the cancer has spread from the prostate farther into the body such as the lungs, liver, or bones, was only 31%

Prostate cancer is easiest to cure when treated before it spreads from the prostate. The URF supports routine screening for the early detection of prostate cancer.

Siegel, R.L., Miller, K.D. and Jemal, A. (2020), Cancer statistics, 2020. CA A Cancer J Clin, 70: 7-30. doi:10.3322/caac.21590

Butler, S.S., Muralidhar, V., Zhao, S.G., Sanford, N.N., Franco, I., Fullerton, Z.H., Chavez, J., D'Amico, A.V., Feng, F.Y., Rebbeck, T.R., Nguyen, P.L. and Mahal, B.A. (2020), Prostate cancer incidence across stage, NCCN risk groups, and age before and after USPSTF Grade D recommendations against prostate specific antigen screening in 2012. Cancer, 126: 717-724. doi:10.1002/cncr.32604

Source URL*: https://drcatalona.com/quest/good-news-overall-complicated-for-prostate-cancer/*

Updated Nutrition Facts Label Reflects Science on Diet and Health, including Cancer

May 19, 2020, by NCI Staff

For more information go to:

https://www.cancer.gov/news-events/cancer-currents-blog/2020/nutrition-facts-label-updated-fda-nci?cid=eb_govdel

Contributions

Our thanks to those who help us continue our outreach

Robert & Alice Barringer
Fred Bell
Robert Miggins
Earl Prochaska
Wm. & Iris Miller
Dan & Margaret Sickles
Your Cause AT&T

Prostate Cancer 101 is a 501 (c) (3) IRS approved non-profit organization. Your ***tax deductible*** donations should be mailed to:

Prostate Cancer 101
c/o Diane Sutkowski,
Treasurer
8 Alcazar Avenue
Kingston NY 12401-4302

We need your donations to help continue our meetings and newsletters.

Liquid Biopsies Lead to Precision Medicine in Prostate Cancer

CAROLINE SEYMOUR

Liquid biopsy with circulating tumor DNA (ctDNA) could help alleviate some of the challenges of tissue biopsy in prostate cancer, and in doing so, lead to a better precision medicine model in the field, according to early evidence from the phase 2 Prostate Cancer Biomarker Enrichment and Treatment Selection (PC-BETS) trial, explained Kim Chi, MD.

In the trial, 250 patients with progressive metastatic castration-resistant prostate cancer (mCRPC) underwent ctDNA screening. A total of 169 patients had 1% or greater ctDNA, and 81 had less than 1% ctDNA. Patients were grouped into 1 of 4 arms, irrespective of biomarker positivity.

Preliminary results from the trial, which were presented at the 2020 ASCO Virtual Scientific Program, showed that 8 patients who were enrolled in the darolutamide (Nubeqa) arm (n = 36) and 1 patient in the adavosertib arm (n = 19) derived clinical benefit.

"There are commercial and research assays out there, and there's a lot of ongoing research on how we can take ctDNA and apply it to our patients, both for prognostic and predictive purposes," said Chi. "Our data show the promise of ctDNA to identify actionable alterations in patients."

In an interview with *Oncology Nursing News*' sister publication, *OncLive*, Chi, senior research scientist, Vancouver Prostate Center, chief medical officer and vice president, BC Cancer, medical oncologist, BC Cancer, and professor, Department of Medicine, University of British Columbia, discussed the results of the PC-BETS study and the untapped potential for targeted therapy in prostate cancer.

OncLive: **What inspired this research?**

Chi: Although we have expanding treatment options for men with CRPC, the disease remains lethal. We also know that there is a long tail on the curve in terms of genomic alterations that could be targeted with novel treatments.

Could you highlight the design of the trial?

We conducted this ongoing phase 2 umbrella study in men with mCRPC who were progressing after next-generation hormone therapy, as well men who were progressing after docetaxel. Patients were enrolled and stratified according to biomarker status. All patients had ctDNA sequencing. Biomarker-positive patients were enrolled by a tumor board using preset criteria to various targeted therapies, and biomarker-negative patients were randomized to any of the open arms.

In the preliminary analysis, we showed that over 250 patients have been screened, and 84 have been enrolled. We see some early activity in the patients who were treated with adavosertib and darolutamide. The safety data was consistent with these agents and what we've seen in the past, so there were no safety concerns.

How might these data augment the field of targeted therapy in prostate cancer?

We recently heard about patients with DNA repair alterations benefitting from agents like PARP inhibitors. Our research is expanding [targeted therapy] to a wider group of patients by asking if there are there other alterations that we can target. We need to work on furthering precision medicine for patients with CRPC.

Why has it been so difficult to develop targeted therapies in prostate cancer compared with other malignancies?

The limiting factor has been tissue. Getting archival tissue or fresh biopsies from patients can be a challenge. In the

PARP inhibitor studies, the assays often fail to provide a result, be it positive or negative. Biopsies can be challenging for patients, especially for those with prostate cancer who have bone metastases. Also, it's not uncommon for there not to be enough cells [to biopsy].

With our approach, we started off using ctDNA right at the start. In patients with advanced prostate cancer, especially after progression after 1 or 2 lines of therapy, the majority have abundant ctDNA for analysis.

Could liquid biopsy become as widespread in prostate cancer as it is in lung cancer?

In lung cancer, you're looking for specific mutations, which can be detected at very low levels of ctDNA. Prostate cancer is a little bit different because we don't have those point mutations that we're looking for. We have to adopt a wider view, so we need larger amounts of ctDNA in order to analyze the [sample] appropriately. In prostate cancer, we have these challenges with the tissue. ctDNA liquid biopsies are really going to play a prominent role in the future of prostate cancer, and even for example, with PARP inhibitors, in identifying patients with DNA repair.

Is there anything else about this study that you want to make sure that people know about?

This is an ongoing study. We're adding additional arms, including an AKT inhibitor, as well as immunotherapy. We will be able to rapidly identify active agents for patients who have actionable alterations.

Reference

Chi KN, Mukherjee S, Saad F, et al. Prostate cancer biomarker enrichment and treatment selection (PCBETS) study: a Canadian cancer trials group phase II umbrella trial for metastatic castration-resistant prostate cancer (mCRPC). J Clin Oncol. 2020;38(suppl 15):5551. doi:10.1200/JCO.2020.38.15_suppl.5551

This article was originally published on OncLive as, "Early Biomarker Data Provide Framework for Precision Medicine-Based Trials in Prostate Cancer."

Source URL: https://www.oncnursingnews.com/web-exclusives/liquid-biopsies-lead-to-precision-medicine-in-prostate-cancer

We are hoping to start meetings in September, but are waiting for the final answer from the Hurley Church. We'll send emails and have an ad in the Freeman if we can meet on Sept. 1.

A Thank you Letter To Gene Groelle

Dear Gene,

How can we all thank you for the two plus decades of wisdom and assistance that you brought to so many men at our First Tuesday meetings. You have been our fountain of knowledge on tried and true protocols and shared with us all what was in the pipeline of clinical trials in new treatments and pharmaceuticals. You did the research and gave solid information, not speculation. We all knew you knew from whence you spoke and said it like and to a friend.

You were there with Ron Koster, John Breithaupt and John Decker almost from the inception of our Kingston group 25 years ago. Our silver anniversary has many to thank for being there in a time of great need. You have been a keystone to our PCa 101 group and deserve a medal for being so steadfast for all that time. I know you don't want or need one, but this note of thanks for all to see might be a good substitute.

Ignatz, thanks for the knowledge you shared, the fun and laughter at dinners at Chez Sutkowski, the words of encouragement and so much more. Your shoes will be hard to fill and may take at least two to accomplish what you have done for us all. May you be well and enjoy years to come. You will be sorely missed.

Love,
Tillie and the Gang

How CRISPR Is Changing Cancer Research and Treatment

Credit: Ernesto del Aguila III, National Human Genome Research Institute July 27, 2020, by NCI Staff

CRISPR is a highly precise gene editing tool that is changing cancer research and treatment.
Ever since scientists realized that changes in DNA cause cancer, they have been searching for an easy way to correct those changes by manipulating DNA. Although several methods of gene editing have been developed over the years, none has really fit the bill for a quick, easy, and cheap technology.

But a game-changer occurred in 2013, when several researchers showed that a gene-editing tool called CRISPR could alter the DNA of human cells like a very precise and easy-to-use pair of scissors.

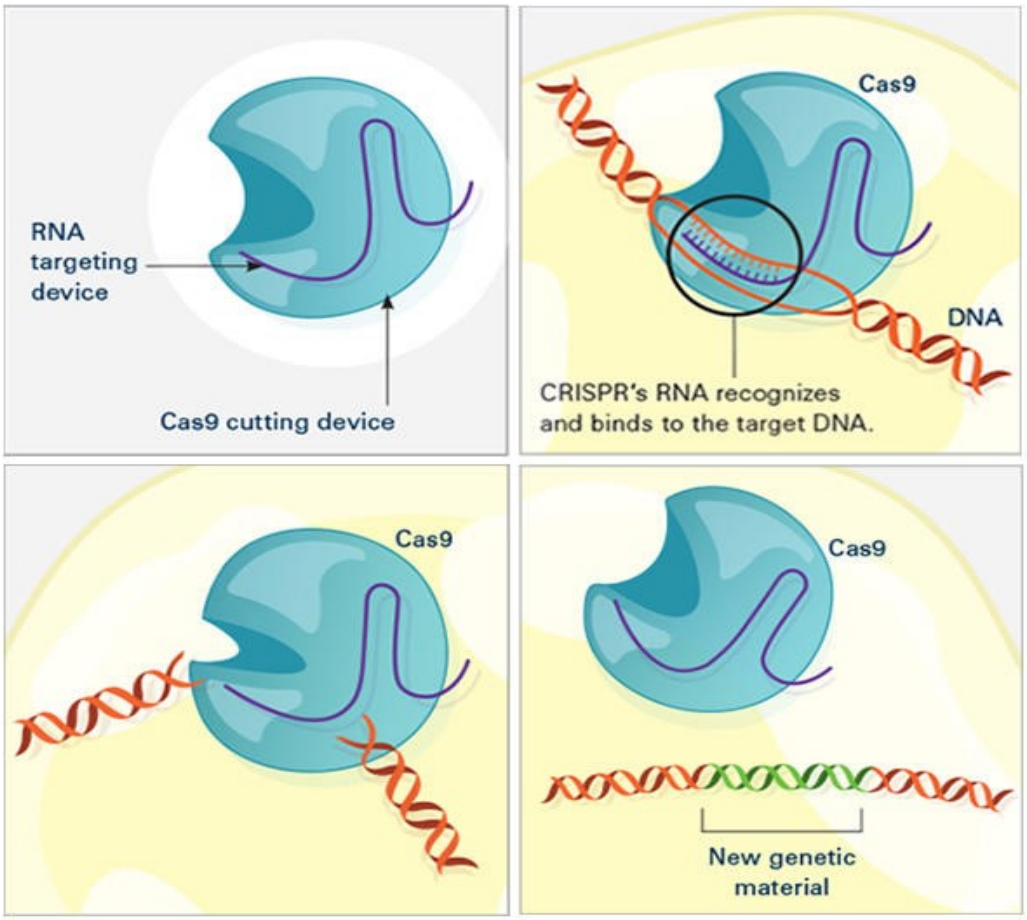
The new tool has taken the research world by storm, markedly shifting the line between possible and impossible. As soon as CRISPR made its way onto the shelves and freezers of labs around the world, cancer researchers jumped at the chance to use it.
"CRISPR is becoming a mainstream methodology used in many cancer biology studies because of the convenience of the technique," said Jerry Li, M.D., Ph.D., of NCI's Division of Cancer Biology.

Now CRISPR is moving out of lab dishes and into trials of people with cancer. In a small study, for example, researchers tested a cancer treatment involving immune cells that were CRISPR-edited to better hunt down and attack cancer.

Despite all the excitement, scientists have been proceeding cautiously, feeling out the tool's strengths and pitfalls, setting best practices, and debating the social and ethical consequences of gene editing in humans.

How Does CRISPR Work?
Like many other advances in science and medicine, CRISPR was inspired by nature. In this case, the idea was borrowed from a simple defense mechanism found in some microbes, such as bacteria. To protect themselves against invaders like viruses, these microbes capture snippets of the intruder's DNA and store them away as segments called CRISPRs, or clustered regularly interspersed short palindromic repeats. If the same germ tries to attack again, those DNA segments (turned into short pieces of RNA) help an enzyme called Cas find and slice up the invader's DNA.

After this defense system was discovered, scientists realized that it had the makings of a versatile gene-editing tool. Within a handful of years, multiple groups had successfully adapted the system to edit virtually any section of DNA, first in the cells of other microbes, and then eventually in human cells.



Enlarge
CRISPR consists of a guide RNA (RNA-targeting device, purple) and the Cas enzyme (blue). When the guide RNA matches up with the target DNA (orange), Cas cuts the DNA. A new segment of DNA (green) can then be added.
Credit: National Institute of General Medical Sciences, National Institutes of Health
In the laboratory, the CRISPR tool consists of two main actors: a guide RNA and a DNA-cutting enzyme, most commonly one called Cas9. Scientists design the guide RNA to mirror the DNA of the gene to be edited (called the target). The guide RNA partners with Cas and—true to its name—leads Cas to the target. When the guide RNA matches up with the target gene's DNA, Cas cuts the DNA.
What happens next depends on the type of CRISPR tool that's being used. In some cases, the target gene's DNA is scrambled while it's repaired, and the gene is inactivated. With other versions of CRISPR, scientists can manipulate genes in more precise ways such as adding a new segment of DNA or editing single DNA letters.

Scientists have also used CRISPR to detect specific targets, such as DNA from cancer-causing viruses and RNA from cancer cells. Most recently, CRISPR has been put to use as an experimental test to detect the novel coronavirus.

Why Is CRISPR a Big Deal?
Scientists consider CRISPR to be a game-changer for a number of reasons. Perhaps the biggest is that CRISPR is easy to use, especially compared with older gene-editing tools.
"Before, only a handful of labs in the world could make the proper tools [for gene editing]. Now, even a high school student can make a change in a complex genome" using CRISPR, said Alejandro Chavez, M.D., Ph.D., an assistant professor at Columbia University who has developed several novel CRISPR tools.

CRISPR is also completely customizable. It can edit virtually any segment of DNA within the 3 billion letters of the human genome, and it's more precise than other DNA-editing tools.
And gene editing with CRISPR is a lot faster. With older methods, "it usually [took] a year or two to generate a genetically engineered mouse model, if you're lucky," said Dr. Li. But now with CRISPR, a scientist can create a complex mouse model within a few months, he said.

Another plus is that CRISPR can be easily scaled up. Researchers can use hundreds of guide RNAs to manipulate and evaluate hundreds or thousands of genes at a time. Cancer researchers often use this type of experiment to pick out genes that might make good drug targets.

And as an added bonus, "it's certainly cheaper than previous methods," Dr. Chavez noted.

What Are CRISPR's Limitations?

With all of its advantages over other gene-editing tools, CRISPR has become a go-to for scientists studying cancer. There's also hope that it will have a place in treating cancer, too. But CRISPR isn't perfect, and its downsides have made many scientists cautious about its use in people.

A major pitfall is that CRISPR sometimes cuts DNA outside of the target gene—what's known as "off-target" editing. Scientists are worried that such unintended edits could be harmful and could even turn cells cancerous, as occurred in a 2002 study of a gene therapy.

"If [CRISPR] starts breaking random parts of the genome, the cell can start stitching things together in really weird ways, and there's some concern about that becoming cancer," Dr. Chavez explained. But by tweaking the structures of Cas and the guide RNA, scientists have improved CRISPR's ability to cut only the intended target, he added.

Another potential roadblock is getting CRISPR components into cells. The most common way to do this is to co-opt a virus to do the job. Instead of ferrying genes that cause disease, the virus is modified to carry genes for the guide RNA and Cas.

Slipping CRISPR into lab-grown cells is one thing; but getting it into cells in a person's body is another story. Some viruses used to carry CRISPR can infect multiple types of cells, so, for instance, they may end up editing muscle cells when the goal was to edit liver cells.

Researchers are exploring different ways to fine-tune the delivery of CRISPR to specific organs or cells in the human body. Some are testing viruses that infect only one organ, like the liver or brain. Others have created tiny structures called nanocapsules that are designed to deliver CRISPR components to specific cells.

Because CRISPR is just beginning to be tested in humans, there are also concerns about how the body—in particular, the immune system—will react to viruses carrying CRISPR or to the CRISPR components themselves.

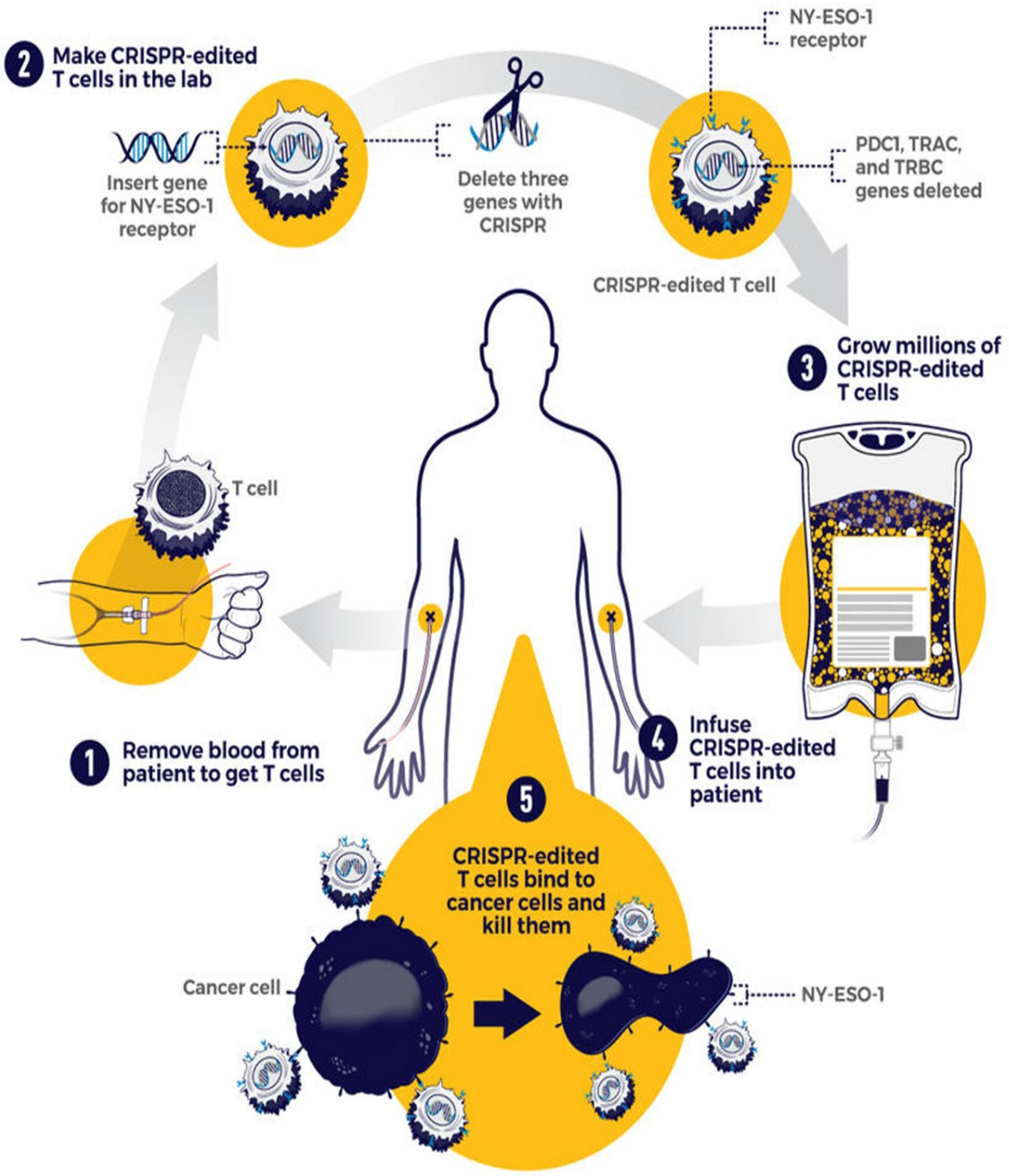
Some wonder whether the immune system could attack Cas (a bacterial enzyme that is foreign to human bodies) and destroy CRISPR-edited cells. Twenty years ago, a patient died after his immune system launched a massive attack against the viruses carrying a gene therapy he had received. However, newer CRISPR-based approaches rely on viruses that appear to be safer than those used for older gene therapies.

Another major concern is that editing cells inside the body could accidentally make changes to sperm or egg cells that can be passed on to future generations. But for almost all ongoing human studies involving CRISPR, patients' cells are removed and edited outside of their bodies. This "ex vivo" approach is considered safer because it is more controlled than trying to edit cells inside the body, Dr. Chavez said.

However, one ongoing study is testing CRISPR gene editing directly in the eyes of people with a genetic disease that causes blindness, called Leber congenital amaurosis.

The First Clinical Trial of CRISPR for Cancer

The first trial in the United States to test a CRISPR-made cancer therapy was launched in 2019 at the University of Pennsylvania. The study, funded in part by NCI, is testing a type of immunotherapy in which patients' own immune cells are genetically modified to better "see" and kill their cancer.


CRISPR-edited T cells
2 Make CRISPR-edited T cells in the lab
Insert gene for NY-ESO-1 receptor
Delete three genes with CRISPR
NY-ESO-1 receptor
PDC1, TRAC, and TRBC genes deleted
CRISPR-edited T cell
3 Grow millions of CRISPR-edited T cells
T cell
1 Remove blood from patient to get T cells
4 Infuse CRISPR-edited T cells into patient
5
CRISPR-edited T cells bind to cancer cells and kill them
Cancer cell
NY-ESO-1

The first trial of CRISPR for patients with cancer tested T cells that were modified to better "see" and kill cancer. CRISPR was used to remove three genes: two that can interfere with the NY-ESO-1 receptor and another that limits the cells' cancer-killing abilities. Credit: National Cancer Institute
The therapy involves making four genetic modifications to T cells, immune cells that can kill cancer. First, the addition of a synthetic gene gives the T cells a claw-like protein (called a receptor) that "sees" NY-ESO-1, a molecule on some cancer cells.

Then CRISPR is used to remove three genes: two that can interfere with the NY-ESO-1 receptor and another that limits the cells' cancer-killing abilities. The finished product, dubbed NYCE T cells, were grown in large numbers and then infused into patients.
"We had done a prior study of NY-ESO-1–directed T cells and saw some evidence of improved response and low toxicity," said the trial's leader, Edward Stadtmauer, M.D., of the University of Pennsylvania. He and his colleagues wanted to see if removing the three genes with CRISPR would make the T cells work even better, he said.

The goal of this study was to first find out if the CRISPR-made treatment was safe. It was tested in two patients with advanced multiple myeloma and one with metastatic sarcoma. All three had tumors that contained NY-ESO-1, the target of the T-cell therapy.

Initial findings suggest that the treatment is safe. Some side effects did occur, but they were likely caused by the chemotherapy patients received before the infusion of NYCE cells, the researchers reported. There was no evidence of an immune reaction to the CRISPR-edited cells.

Only about 10% of the T cells used for the therapy had all four of the desired genetic edits. And off-target edits were found in the modified cells of all three patients. However, none of the cells with off-target edits grew in a way that suggested they had become cancer, Dr. Stadtmauer noted.
The treatment had a small effect on the patients' cancers. The tumors of two patients (one with multiple myeloma and one with sarcoma) stopped growing for a while but resumed growing later. The treatment didn't work at all for the third patient.
It's exciting that the treatment initially worked for the sarcoma patient because "solid tumors have been a much more difficult nut to crack with cellular therapy," Dr. Stadtmauer said. "Perhaps [CRISPR] techniques will enhance our ability to treat solid tumors with cell therapies."

Although the trial shows that CRISPR-edited cell therapy is possible, the long-term effects still need to be monitored, Dr. Stadtmauer continued. The NYCE cells are "safe for as long as we've been watching [the study participants]. Our plan is to keep monitoring them for years, if not decades," he said.

More Studies of CRISPR Treatments to Come

While the study of NYCE T cells marked the first trial of a CRISPR-based cancer treatment, there are likely more to come.
"This [trial] was really a proof-of-principle, feasibility, and safety thing that now opens up the whole world of CRISPR editing and other techniques of [gene] editing to hopefully make the next generation of therapies," Dr. Stadtmauer said.
Other clinical studies of CRISPR-made cancer treatments are already underway. A few trials are testing CRISPR-engineered CAR T-cell therapies, another type of immunotherapy. For example, one company is testing CRISPR-engineered CAR T cells in people with B cell cancers and people with multiple myeloma.

There are still a lot of questions about all the ways that CRISPR might be put to use in cancer research and treatment. But one thing is for certain: The field is moving incredibly fast and new applications of the technology are constantly popping up.

"People are still improving CRISPR methods," Dr. Li said. "It's quite an active area of research and development. I'm sure that CRISPR will have even broader applications in the future."

< Older Post

Liquid Biopsy Detects Brain Cancer and Early-Stage Kidney Cancer
Newer Post >

How Does Ovarian Cancer Form? A New Study Points to MicroRNA

Source URL: https://www.cancer.gov/news-events/cancer-currents-blog/2020/crispr-cancer-research-treatment?cid=eb_govdel

New Focus on ADT in Prostate Cancer Guideline
-AUA, SUO, ASTRO offer 38 recommendations across categories of advanced disease

by Charles Bankhead, Senior Editor, MedPage Today June 30, 2020

For the first time in its long and storied history, hormonal therapy for advanced prostate cancer has received broad and detailed attention in a clinical practice guideline.

The new American Urological Association (AUA) guideline provides direction for the use of hormonal therapy (or androgen-deprivation therapy, ADT) for men with multiple categories of advanced and metastatic prostate cancer.

"[ADT] is a mainstay of management that we've known about since the Nobel Prize-winning work in the 1940s," said guideline co-chair Michael Cookson, MD, of the University of Oklahoma Health Sciences Center in Oklahoma City. "It's taken a long time to get there, and that's partly due to the fact that a lot of what we did was empiric. There weren't many trials designed to show the true benefit."

Another guideline first reflects the growing recognition of the different stages of disease evolution before the emergence of metastatic castration-resistant prostate cancer (mCRPC).
"There's a lot of excitement in the field about newly diagnosed metastatic disease," Cookson told *MedPage Today*. "Most of the early trials were in men who failed hormonal therapy. Now the trials have moved back to earlier in the disease, looking at conventional hormonal therapy, *plus*. That 'plus' initially included chemotherapy, which showed survival advantages of 12 to 18 months. That was big.

"Then additional androgen-active therapies, such as abiraterone (Zytiga) and then oral agents such as enzalutamide (Xtandi) and now apalutamide (Erleada). That translated into a year or more of additional cancer control and survival when the disease was treated earlier with the combination," he said.

The guideline also addressed the evolutionary period before emergence of radiographically confirmed mCRPC, often associated with a rapid rise in prostate-specific antigen (PSA). Now known as non-metastatic CRPC, the disease state has three FDA-approved options in the androgen receptor antagonist drug class: darolutamide (Nubeqa), in addition to enzalutamide and apalutamide. The drugs' approval was based primarily on the newly recognized endpoint of metastasis-free survival and relatively limited overall survival data, said Cookson. Subsequently, a survival advantage was reported for enzalutamide.

"That's been a real area of controversy," he continued. "Many clinicians were hesitant to fully embrace the therapy because they didn't really understand the true benefit of this new endpoint called metastasis-free survival. The 'purists' among oncologists, and maybe just the purists in general, want an overall survival benefit. Now we're starting to see that happen. There are three studies in that category, and as the data matures, I think we'll see more of that, since the drugs are pretty similar."

Frontline standard of care for mCRPC remains docetaxel for men with no prior exposure to the drug. Cabazitaxel (Jevtana) or a novel antiandrogen agent is appropriate in the setting of docetaxel failure.

New to guideline history -- and to many clinicians who treat prostate cancer -- is genetic testing. About a fourth of CRPC harbors germline or somatic mutations, said Cookson. New drugs that target the mutations continue to emerge on a regular basis, affording opportunities for precision-medicine approaches to treatment of CRPC. The most common mutation is *BRCA2*, and the FDA has already approved two drugs to treat CRPC harboring

BRCA2 mutations, the PARP inhibitors olaparib (Lynparza) and rucaparib (Rubraca).

"There are instances in which men have been on conventional therapy -- chemotherapy or hormonal therapy -- and they've also failed the newer antiandrogens, such as abiraterone and enzalutamide," said Cookson. "In the past, we didn't have much hope for them. Now there is a class of drugs that if they have the right genetic makeup in their tumor, they're going to have a better chance to respond to the therapy."

Immunotherapy may also have a role for some men with CRPC. The PD-1 inhibitor pembrolizumab (Keytruda) has tumor-agnostic approval for treatment of heavily mutated solid tumors (microsatellite instability-high). The field of prostate cancer is "still in its infancy" with regard to use of drugs that target genetic alterations in tumors.

The key message in the guideline is for prostate cancer specialists to be aware of recommendations for genetic testing, particularly for men with aggressive disease that progresses rapidly through conventional therapies, Cookson added. Moreover, testing for germline mutations has implications for genetic counseling, including family members who might be at increased risk for several types of cancer.

The guideline was developed in collaboration with the Society of Urologic Oncology and the American Society for Radiation Oncology. The guideline panel made a total of 38 recommendations pertaining to the the prostate cancer continuum of care:

- Early evaluation and counseling
- Nonmetastatic biochemical recurrence after exhaustion of local treatment options
- Metastatic hormone-sensitive prostate cancer
- Nonmetastatic CRPC
- mCRPC

Bone health

The complete guideline is available on the AUA website. Cookson and the other guideline co-chair, William Lowrance, MD, of the University of Utah School of Medicine and the Huntsman Cancer Institute in Salt Lake City, summarized the key points of the guideline during the AUA virtual meeting.

"For the past several years, the prostate cancer landscape has been rapidly evolving due to changes in PSA screening standards, as well as the approval of new classes of treatment options for use in various prostate cancer disease states," Lowrance said in a statement. "This guideline is comprised of clinical recommendations based on this new evidence and aims to further support the medical community and patients as they navigate through the various stages of this disease."

Charles Bankhead is senior editor for oncology and also covers urology, dermatology, and ophthalmology. He joined MedPage Today in 2007. Follow

Disclosures

Cookson disclosed relationships with TesoRx Pharma, Astellas, Merck, Bayer, Ferring, and Myovant; Lowrance disclosed relationships with Myriad Genetics and Stream Dx; several other members of the guideline panel also disclosed relationships with various commercial and noncommercial organizations.

Primary Source

American Urological Association

Source Reference: Lowrance W, et al "Advanced prostate cancer: AUA/ASTRO/SUO Guideline" *AUA* 2020.

Source URL: https://www.medpagetoday.com/meetingcoverage/aua/87354

Prostate Cancer 101, Inc.
8 Alcazar Avenue
Kingston, NY 12401-4302

1st Tuesday

4:30 p.m. monthly

SEMINAR
For
Newly Diagnosed

Hurley Reformed Church Hall, Hurley, NY

Membership and Administration

If you have *moved*, have a *new email* or *phone* or *no longer wish to receive the newsletter*, please let us know.

It's up to you to keep us informed so we can keep you informed.

Diane Sutkowski
845-331-7241
dsutkowski@hvc.rr.com

PCa 101 Seminar
First Tuesday of every month

Gene Groelle 845-419-5128
Gro226@aol.com

Arlene Ryan 338-9229
ryanarlene918@gmail.com

Walt Sutkowski 331-7241
wsutkowski@hvc.rr.com

Diane Sutkowski 331-7241
dsutkowski@hvc.rr.com

Website & Newsletters

http://prostatecancer101.org

Walt Sutkowski
845-331-7241
wsutkowski@hvc.rr.com

Prostate Cancer 101 is a 501(c) (3) IRS approved non-profit organization