Newsletter

Prostate Cancer 101, Inc.

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

4 in 10 Believe Alternative Therapies Cure Cancer

By Robert Preidt
HealthDay Reporter

TUESDAY, Oct. 30, 2018 (HealthDay News) -- Despite evidence to the contrary, four in 10 Americans believe alternative therapies can cure cancer, a new survey finds.

Research shows that cancer death rates are much higher among patients who use only alternative therapies than among those who receive standard cancer treatments, according to the American Society of Clinical Oncology (ASCO).

The group's second annual National Cancer Opinion Survey also found that many Americans oppose limiting cancer patients' access to opioid painkillers (such as OxyContin) and support the use of medical marijuana by cancer patients.

The high cost of cancer also emerged as a major concern among Americans.

"This survey serves as a barometer of the American people's views on important cancer-related issues," said ASCO President Dr. Monica Bertagnolli.

"It's revealed a number of critical areas we urgently need to address -- from correcting widespread misinformation about cancer treatments, to ensuring patients have access to the pain medication they need, to alleviating the financial distress both patients and their loved ones experience too frequently," Bertagnolli said in a society news release.

The online survey, conducted in July and August, included almost 4,900 U.S. adults aged 18 and older. About 1,000 have or have had cancer.

The survey found that 39 percent of respondents -- including a high number of cancer patients and family caregivers -- believe cancer can be cured using just alternative therapies, such as enzyme and oxygen therapy, diet, vitamins and minerals.

According to ASCO Chief Medical Officer Dr. Richard Schilsky, "There's no question that evidence-based cancer therapy is necessary to effectively treat the disease."

He added: "The vast majority of alternative therapies either haven't been rigorously studied or haven't been found to benefit patients. When patients are making critical decisions about which cancer treatments to undergo, it is always best to follow the evidence from well-designed research studies."

Younger people -- between 18 and 53 -- were more likely to put their faith in alternative therapies, the survey revealed.

A recent study in the *Journal of the National Cancer Institute* underscored the danger of such thinking: The death rate from common cancers for people who receive only alternative medicine treatments is 2.5 times higher than for patients who receive standard treatments, such as surgery, radiation, chemotherapy, immunotherapy and hormone-based therapies.

Other findings from the ASCO survey:

- Nearly three-quarters of the respondents said new regulations that make prescription opioids harder to obtain should not apply to cancer patients.

Forty percent of cancer patients who have used opioids in the past 12 months to manage pain or other symptoms have had trouble obtaining the medications.

More than eight out of 10 re-

spondents support use of medical marijuana by cancer patients. But 48 percent of cancer patients who have used medical marijuana in the past 12 months said they had trouble obtaining it.

If diagnosed with cancer, 57 percent said their chief concern would be the financial impact on their families or the cost of treatment. Dying or concerns about cancer-related pain and suffering would be the key worry for a smaller percentage (54 percent each).

"Patients are right to be concerned about the financial impact of a cancer diagnosis on their families. It's clear that high treatment costs are taking a serious toll not only on patients, but also on the people who care for them," Schilsky said. "If a family member has been diagnosed with cancer, the sole focus should be helping them get well," Schilsky said. "Instead, Americans are worrying about affording treatment, and in many cases, they're making serious personal sacrifices to help pay for their loved ones' care."

WebMD News from HealthDay

Sources

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https://www.webmd.com/cancer/news/20181030/4-in-10-believe-alternative-therapies-cure-cancer?ecd=wnl_can_110618&ctr=wnl-can-110618_nsl-Bodymod-ule_Position1&mb=IHb0bPtGTXzn%2fZ72N%2fgTKuBPk9ElyaPiRLJhlZSwcrw%3d#1

3 in 4 Men with Slow-growing Prostate Cancer Fail to Get Appropriate Follow-up, Study Finds

August 13, 2018
by Marta Figueiredo

Nearly three-quarters of men with slow-growing prostate cancer who decide on active surveillance are not receiving the appropriate follow-up and might be missing signs of tumor worsening, according to a recent retrospective study from Australia.

The study, "Active surveillance of men with low risk prostate cancer: evidence from the Prostate Cancer Outcomes Registry–Victoria," was published in the *Medical Journal of Australia*.

Prostate cancer is the second most common cancer in men worldwide after skin cancer. Most localized prostate cancer is slow-growing and slow to spread — called low-risk prostate cancer — and may not need treatment or shorten a man's life.

Because of that, active surveillance, a monitoring option that allows the screening of any signs of tumor growth or worsening before surgical removal or therapy, is highly recommended in these cases.

This way, if the cancer does not progress, patients can avoid unnecessary invasive surgery and other burdensome treatments that might have side effects.

About 70% of men with low-risk prostate cancer who adhere to active surveillance will not need additional treatment, whereas the other 30% will have disease progression.

But even though these patients have a low risk of cancer progression and spread, it is essential that they are closely monitored through active surveillance, consisting of periodic biopsies of prostate tissue and blood tests to assess prostate specific antigens (PSA).

The numbers of patients adhering to accepted active surveillance protocols has increased over the years. Sweden may currently hold the highest percentage of patients opting for it, at 74%. However, less than 30% of patients in Europe and less than 13% in the U.S. have been reported to have the appropriate follow-up measures.

To assess how many of these prostate cancer patients in Victoria, Australia, fully adhere to active surveillance, their characteristics, and the factors associated with good adherence, researchers analyzed data from the Prostate Cancer Outcomes Registry–Victoria (PCOR-Vic).

The PCOR-Vic was established in 2009 to improve knowledge about treatments and outcomes for men diagnosed with prostate cancer in the state of Victoria, Australia.

Researchers analyzed the data of 1,635 men age 75 or younger at diagnosis, between August 2008 and December 2014, whose cancer was classified as grade group 3 or less as determined by the International Society of Urological Pathology (ISUP), and managed through active surveillance for at least two years.

The accepted active surveillance follow-up protocol was defined as at least one follow-up biopsy and three PSA blood tests over a two-year period.
Patients' mean age at diagnosis was 64; 1,222 (74.7%) were diagnosed through transrectal ultrasound guided (TRUS) biopsy, and 1,102 (84%) had prostate cancer classified as ISUP grade group 1 (the most favorable disease state).

Only 433 patients (26.5%) followed the appropriate active surveillance protocol, leaving 1,202 men (73.5%) at a higher risk of missing a potential cancer progression.
Among all participants, 877 (53.6%) had at least one follow-up biopsy, and 601 (36.8%) underwent at least three PSA blood tests, while biopsy and PSA assessment were not conducted in 626 men (38.3%) and 80 (4.9%), respectively, within the two years after diagnosis.

Additional analysis showed that men diagnosed in private hospitals were more likely to fully adhere to adequate active surveillance than those diagnosed in public hospitals. Among the factors associated with poor adherence were diagnosis through transurethral resection of the prostate (TURP) or transperineal biopsy (compared with TRUS biopsy), and being 66 or older at diagnosis (compared with younger than 55).

The team noted that additional studies to better understand the reasons behind poor adherence are needed, as well as an education campaign for patients and doctors highlighting the importance of active surveillance in these patients.

Marta Figueiredo

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Ovarian Cancer Treatment Named Breakthrough Therapy with Potential in Advanced Prostate Cancers October 8, 2018

 by Alejandra Viviescas, PhD.

An approved therapy for advanced ovarian cancer — Rubraca (rucaparib) by Clovis Oncology — has been designated a breakthrough therapy by the U.S. Food and Drug Administration as a potential treatment for metastatic castration-resistant prostate cancer (mCRPC) patients with BRCA mutations.

This FDA designation is given to speed the development of medications that might treat serious conditions and potentially provide an improvement on available therapies.
"We hope the decision by the FDA to grant this Breakthrough Therapy designation for Rubraca offers encouragement to the prostate cancer community, and we will do our best to make Rubraca available to eligible prostate cancer patients as quickly as possible," Patrick J. Mahaffy, president and CEO of Clovis Oncology, said in a press release.

About a quarter of advanced prostate cancers show mutations in *BRCA1*, *BRCA2* or other genes encoding proteins that repair damaged DNA. These tumors are more sensitive to further DNA damage, and often respond well to treatments that block other proteins involved in DNA repair.
Rubraca is an oral medicine that inhibits PARP1, PARP2, and PARP3 enzymes, which play a key role in DNA repair when the BRCA proteins are not functioning properly.

The FDA based its decision on preliminary results from TRITON 2 study, which will be presented for the first time at the European Society for Medical Oncology (ESMO) 2018 Congress in Munich, and at the 25th Annual Scientific Retreat of the Prostate Cancer Foundation in Carlsbad, California, later this month.

The Phase 2 trial (NCT02952534) is testing the efficacy and safety of Rubraca (600 mg twice a day) in mCRPC patients who have inherited or acquired BRCA mutations, and who were already treated with androgen receptor-directed therapy and taxane-based chemotherapy.

Its primary goal is to determine the proportion of patients who respond to Rubraca, and those who achieve a significant lowering of their PSA levels. Secondary measures include duration of response, time to disease progression or death, and overall survival.

"We are pleased the FDA has granted Breakthrough Therapy designation to Rubraca in mCRPC," said Howard R. Soule, PhD, executive vice president and chief scientific officer of the Prostate Cancer Foundation.

"There is tremendous need for new therapeutic options in advanced prostate cancer. In particular, we are enthusiastic about the potential for targeted therapies that may provide more meaningful benefits to patients with specific genetic mutations," Soule added.

Enrollment in TRITON2 is ongoing. The trial expects to evaluate about 160 patients from at least 100 worldwide locations, and to study other mutations besides BRCA1/2.

Rubraca was approved by the FDA in April as a maintenance treatment for people with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.

Source URL: https://prostatecancernewstoday.com/2018/10/08/ovarian-cancer-treatment-rubraca-named-breakthrough-therapy-for-advanced-prostate-cancer-potential/

Happy Hanukkah

Extra! Extra!
Read all about it

Frank Guido, our wonderful restaurateur friend and benefactor, has written an entertaining book called "**Been There, Done That!"** which is available at Little Italy and even at Mariner's Harbor. Walt and I just got our autographed copy the other day and were pleasantly and beautifully surprised to see our own Prostate Cancer 101 organization mentioned several times in a very positive way.

Thank you, Frank. You keep proving how good a person you are, over and over again.

Now be sure and get your own copy ($25.00) so you can enjoy it as much as we are. It is a fun trip down memory lane for all those who were born and bred in the Kingston area and even for those of us who came from elsewhere, not to mention the wealth of photos. I started reading and remembering similarities in my own upbringing – nicknames, family friendships, having a soda at a bar with my uncle when I was just a small kid, absolute respect for our elders and ever so much more.

Frank, you are the best, may you live and enjoy life in good health. Che tu possa vivere 100 anni!

Baylor Research Team Gets $6.3M to Study Disparities Among Minorities with Pro state, Breast Cancers

October 22, 2018 by Mary Chapman

The National Cancer Institute (NCI) has awarded a Baylor College of Medicine research team $6.3 million to develop patient-derived mouse models aimed at understanding the biological reasons behind racial and ethnic health disparities in prostate and breast cancers.

In particular, the funding will help Baylor establish a Minority Patient-derived Xenograft Development and Trial Center (M-PDTC), which will include Baylor and MD Anderson Cancer Center experts specializing in developing patient-derived xenograft (PDX) models, molecular biology and signaling pathways, treatment studies in animals, and pathology and clinical management of prostate and breast cancer.

Patient-derived xenografts are basically disease mouse models created using patients' own tumor cells, which are then implanted into mice and used to study tumor environment or response to specific treatments.

Funded as part of the Beau Biden Cancer Moonshot Initiative, the center will be directed by Nicholas Mitsiades, MD, PhD, associate director of the Center for the Biology of Health Disparities and co-leader of Baylor's Nuclear Receptor Program. He is also associate professor of medicine-hematology at Baylor.

"While socioeconomic and environmental factors definitely contribute to racial and ethnic cancer health disparities, there is also evidence for biological differences, and Baylor is a leader in their study," Mitsiades, said in a press release, noting that many of Baylor's patients are Houston-area minorities.

Prostate cancer is the second-leading cause of death overall for men in the United States, but the mortality rate, for reasons largely unknown, is 2.5 times higher for African-Americans than whites.

The hope is that, with newly established tools, the center will result in better healthcare and access for underserved minority populations nationwide.

Baylor's long collaborative research history and existing infrastructure, along with its healthcare role in the local minority community, makes it a natural fit for the M-PDTC, Mitsiades said.

For instance, Michael Ittmann, MD, PhD, a renowned leader in cancer biology who has spent years investigating health disparities, will be one of the center's co-leaders. Ittmann, the William D. Tigertt Baylor Professor of Pathology at Baylor, recently received a Prostate Cancer Foundation grant to study prostate cancer in black veterans, including those exposed to chemicals used in combat, such as Agent Orange.

Salma Kaochar, PhD, an assistant professor of medicine at Baylor, will lead prostate PDX generation in the center. In partnership with Ittmann and Mitsiades, she has been working to interpret the epigenetic elements — compounds that change how genes are produced without modifying their sequence — of prostate cancer in African-American men.

In addition, Baylor has a prominent role in a $26.5 million NCI and National Institute on Minority Health and Health Disparities study on the roles of genetics, tumor markers, and social stress among blacks with prostate cancer.

The center will also complement the work of Baylor's Lester and Sue Smith Breast Cancer Center and its recently funded PDX Development and Trials Center for Breast Cancer, both part of NCI-PDXNet, an NCI program created to assist in the development and testing of therapies in patient-derived models.

In addition to Mitsiades and Ittmann, center research will also be led by Bert O'Malley, MD, Matthew Ellis, PhD, and Susan Hilsenbeck, PhD. The team will be joined by Nora Navone, MD, PhD, of MD Anderson.

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https://prostatecancernewstoday.com/2018/10/22/baylor-research-team-gets-grant-study-cancer-disparities-minorities/

Rubraca Shrank Tumors in Nearly Half of Advanced Prostate Cancer Patients with BRCA Mutations

October 24, 2018 by Ines Martins, PhD

Rubraca (rucaparib), Clovis Oncology's PARP inhibitor, shrank tumors in 44% of metastatic castration-resistant prostate cancer (mCRPC) patients with *BRCA* mutations included in a Phase 2 clinical trial, the company announced. The treatment, which already is approved for ovarian cancer, also reduced PSA levels — a biomarker of prostate cancer — in 51.1% of patients with *BRCA* mutations.

The findings were presented recently at the European Society of Medical Oncology (ESMO) 2018 Congress by Wassim Abida, a medical oncologist at the Memorial Sloan Kettering Cancer Center, and principal investigator for the Phase 2 study.

The poster was titled "Preliminary results from TRITON2: a phase 2 study of rucaparib in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) associated with homologous recombination repair (HRR) gene alterations."

Nearly 12% of men with mCRPC have a mutation in the *BRCA1* or *BRCA2* genes, which play key roles in repairing errors in the DNA. These tumors are more sus-

ceptible to further DNA damage, and often respond well to treatments that block other proteins involved in DNA damage repair.
The PARP enzymes are at play when BRCA proteins are not functioning properly, and PARP inhibitors have shown great promise in breast and ovarian cancer patients with *BRCA* mutations.

Now, data from the TRITON2 Phase 2 trial (NCT02952534) shows that Rubraca also is effective in prostate cancer patients with such mutations.

"Rubraca has previously demonstrated antitumor activity in its approved indications for women with advanced ovarian cancer," Abida said in a press release. "These new data show that Rubraca may also offer a new approach for the treatment of mCRPC associated with *BRCA1* and *BRCA2* alterations, with the potential to achieve a clinical response in patients with few remaining therapy options."

The trial included 85 mCRPC patients who had received at least one treatment blocking the androgen receptor and one taxane-based chemotherapy, and who had an inherited or acquired mutation in *BRCA* genes or in one of the 13 DNA repair genes known to increase susceptibility to PARP inhibitors.

Depending on their disease and mutation status, patients were divided in three groups: those with *BRCA* or *ATM* mutations and with measurable disease; those with *BRCA* or *ATM* mutations without measurable disease; and those with mutations in other DNA repair genes, with or without measurable disease.
The study's primary objectives were to determine overall response rates in patients with measurable disease, and the proportion of patients without measurable disease who saw a reduction in the PSA levels after treatment.

Secondary goals included duration of response, time to disease progression or death, overall survival, and safety measures.
After a median follow-up of 5.7 months, 46 patients were evaluable for responses. Among the 25 patients with *BRCA* mutations, 44% had seen their tumor shrink, after only a median of 3.7 months on treatment. At the time of the analysis, more than half of patients were still responding to Rubraca.

The results also showed that 51.1% of patients with *BRCA* mutations saw a reduction in their PSA levels.

The most common adverse events were fatigue, nausea, anemia, and constipation. Five patients discontinued Rubraca due to a treatment-related adverse effect, and one patient died of disease progression.
Findings from the trial have led the U.S. Food and Drug Administration to grant breakthrough therapy designation to Rubraca as a treatment for mCRPC patients with *BRCA* mutations, earlier this month.

"We are very encouraged by these initial findings from the TRITON2 study, which demonstrate the potential of Rubraca to treat men with advanced prostate cancer whose disease has progressed after receiving multiple prior lines of therapy," said Patrick J. Mahaffy, president and CEO of Clovis Oncology.

"PARP inhibitors are now a validated therapeutic class in oncology in multiple tumor types, and these new data underscore the benefit that Rubraca may provide for men with advanced, *BRCA*-mutant castration-resistant prostate cancer," Mahaffy added. "Having recently received Breakthrough Therapy designation based on these data, we are committed to the rapid development of Rubraca for men with this very difficult-to-treat disease."

Ines Martins, PhD

Inês Martins holds a BSc in Cell and Molecular Biology from Universidade Nova de Lisboa and is currently finishing her PhD in Biomedical Sciences at Universidade de Lisboa. Her work has been focused on blood vessels and their role in both hematopoiesis and cancer development.

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https://prostatecancernewstoday.com/2018/10/24/rubraca-shrank-tumors-41-percent-mcrpc-patients-with-brca-mutations/

Surgery Plus Radiation Therapy Best at Extending Survival in Locally Advanced Prostate Cancer Patients, Study Says

October 4, 2018 by Ines Martins, PhD

A combination of surgery and radiation therapy is better at extending the survival of men with locally advanced prostate cancer than radiation therapy plus hormone therapy, but is associated with higher rates of erectile dysfunction and urinary incontinence, a study found.

These are the two combinations recommended for high-risk prostate cancer, but the study also shows that only 30 percent of men are getting them.

The study, "Comparative Effectiveness of Radical Prostatectomy With Adjuvant Radiotherapy Versus Radiotherapy Plus Androgen Deprivation Therapy for Men With Advanced Prostate Cancer," was published in the journal *Cancer*.

Despite increased screening availability, nearly one in 10 men will be diagnosed with locally advanced or regionally advanced prostate cancer, a kind of cancer that is growing but has not yet spread to other areas of the body.

These men are at high risk for metastasis and current guidelines recommend they receive a combination treatment that includes either radical prostatectomy (surgical removal of the prostate) followed by radiation therapy, or radiation therapy plus androgen deprivation therapy (a treatment that reduces the levels of male hormones).

But there is no consensus as to which approach is most effective.

So, researchers reviewed the medical records of 13,856 men with locally advanced prostate cancer who were included in the Surveillance, Epidemiology, and End Results (SEER)–Medicare database from 1992 to 2009. Patients were 65 or older and were followed for a median of 14.6 years.

Interestingly, researchers found that half of these patients received single treatment with surgery, radiation, or hormone therapy, rather than a combination therapy. Only 30% of men were receiving any of the recommended combinations, including 6.1% who received the surgery option, and 23.6% who got the radiation plus hormone therapy.

And among those receiving surgery and radiation therapy, 30% also received hormone therapy, researchers said.

Because surgery is seen as a high-risk procedure, with increased risk for urinary incontinence and sexual dysfunction, its use decreased significantly over time, from 9.4% in 1992-1997 to 4% in 2004-2009.

"Prostatectomy is an unpopular treatment," Grace Lu-Yao, PhD, senior author and associate director of Population Science at the Sidney Kimmel Cancer Center-Jefferson Health, said in a press release. "Our study showed that only six percent of men with high-risk cancer were treated with it."

Researchers then compared the outcomes of men treated with either surgery and radiation or radiation and hormone therapy. Patients were matched by age, race, and number of other co-occurring diseases to control for factors that could influence their outcomes.

The team found that after 10 years, 88.9% of men who received surgery were still alive, compared to 74.2% of those who received the radiation and hormone therapy. However, consistent with prior reports, more of these patients developed urinary incontinence (49.1% vs. 19.4%) and erectile dysfunction (28.3% vs. 20.4%).

"There's a lot of debate about whether to remove the whole prostate and follow up with radiation therapy. Or, as a second option, to spare the prostate and treat it using radiation therapy plus hormone-blocking therapy," said Lu-Yao. "Our study suggests that removing the prostate followed by adjuvant radiotherapy is associated with greater overall survival in men with prostate cancer."

"These findings should be verified with prospective trial data and suggest the need to include a surgical arm in future trials for men with high-risk prostate cancer," the researchers concluded.

Ines Martins, PhD

Inês Martins holds a BSc in Cell and Molecular Biology from Universidade Nova de Lisboa and is currently finishing her PhD in Biomedical Sciences at Universidade de Lisboa. Her work has been focused on blood vessels and their role in both hematopoiesis and cancer development.

Source URL: https://prostatecancernewstoday.com/2018/10/04/surgery-plus-radiation-best-locally-advanced-prostate-cancer-study-says/

Stereotactic Radiation Shows Ability to Significantly Extend Survival in Cancer Patients with Multiple Metastasis

October 26, 2018 by Ines Martins, PhD

Patients whose cancer returns at multiple sites after treatment — called oligometastatic cancer — are generally thought incurable, but a recent Phase 2 trial found that a highly precise form of radiation can significantly extend these patients' lives if the spread shows small tumors, without diminishing life quality.

The approach was tested in patients with up to five metastatic sites, and doubled the time a patient lived without disease progression.

The findings will be presented next week at the American Society for Radiation Oncology (ASTRO) 2018 Annual Meeting. David Palma, MD, PhD, a researcher at Lawson Health Research Institute – the research institute of London Health Sciences Centre (LHSC) and lead institution of the multi-center study – will be presenting the research.

"Traditionally, when a patient had a cancer that spread to other parts of their body—such as to their bones or brain—they were considered to be incurable," Palma said in a press release. "But there's a theory—called the oligometastatic theory—that if a patient only has a few spots of cancer returning, those spots could be killed with radiation or surgery to improve their survival."

Stereotactic ablative body radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), is a kind of precision radiation therapy that uses small, thin beams of radiation directed into the tumor from different angles. The treatment delivers high radiation doses, requiring only one or a few sessions, and because it's precise, healthy tissues nearby are spared.

Given the significant reduction in side effects compared to older radiation therapy approaches, researchers hypothesized the SABR could be used to ablate multiple metastatic lesions in cancer patients.

They designed a Phase 2 trial, called SABR-COMET (NCT01446744), that compared SABR with standard radiation approaches in patients whose cancer had been controlled but returned in up to five distinct locations.

The study included 99 patients from Canada, Scotland, the Netherlands, and Australia, whose most common cancers included breast (18%), lung (18%), colon or rectum (18%), and prostate tumors (16%); all had a life expectancy of more than six months. The majority of patients (93%) had their cancer spread to one to three new sites.

Patients in the trial (median age 68, 59% men) were randomly assigned SABR – given every other day for one to three weeks, depending on the disease site – or palliative radiation therapy. For each patient receiving standard of care, two were given SABR. Patients in both groups were allowed to receive concomitant chemotherapy, at the discretion of the medical oncologist.

Researchers found that SABR significantly extended patients' lives by more than one year. While those receiving this approach lived for a median of three years and five months, patients on palliative radiation therapy lived two years and four months.

Stereotactic radiation also doubled the time patients lived without their disease progressing from six to 12 months. Interestingly, the survival benefits didn't appear to take a toll on quality of life, as patients reported similar scores for physical, social, functional, and emotional scales.

Five years after treatment, nearly half (46%) of patients who received SABR were still alive, which was nearly double the 24% seen in patients receiving palliative radiation.

"We were surprised and quite pleased. We didn't expect the survival benefit to be quite so long for patients with metastatic disease," said Palma, also a clinician-scientist at the Ontario Institute for Cancer Research, which provided funding for this study.

Severe side effects were more common among those receiving SABR (30%) than in patients given standard of care (9%). The most common were fatigue, difficulty breathing, and pain. Three patients died due to SABR-related adverse events.

"Stereotactic radiation therapy needs to be delivered carefully

and by an experienced team, and there is a small risk of very serious side effects, as well as mortality. But overall, for patients whose cancers have spread, and who are not expected to survive otherwise, the overall survival benefit of SABR appear[s] to outweigh these risks," said Palma.
During the trial, some patients developed more lesions that were also successfully treated. Researchers are now designing a follow-up trial, called SABR-COMET-10, that will test the approach in patients with as much as 10 metastatic lesions.

"We don't know the upward limit of how many tumors can be treated with SABR," Palma said. "The concern is the amount of radiation exposure a patient can tolerate. We don't know yet what the safe boundaries are. We've been very conservative, as this is a new technology."

Ines Martins, PhD

Inês Martins holds a BSc in Cell and Molecular Biology from Universidade Nova de Lisboa and is currently finishing her PhD in Biomedical Sciences at Universidade de Lisboa. Her work has been focused on blood vessels and their role in both hematopoiesis and cancer development.

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Tumor fighting Protein, PTEN, Restored in Mice Prostate Cancer Models Using mRNA and Nanoparticles

September 27, 2018 by Joana Carvalho

Messenger RNAs encoding for the PTEN protein that were carried in tiny nanoparticles to prostate cancer cells in a proof-of-concept study were able to destroy those cells, preventing tumor growth and progression in several mouse models of prostate cancer, researchers report.

PTEN is a potent and well-characterized tumor-suppressor protein, and one encoded by a gene that is lost or mutated in about half of all advanced prostate cancers — aiding tumor cells in growing unchecked. Messenger RNAs (mRNAs) are molecules that contain instructions to make proteins.

The study's findings, "Restoration of tumor-growth suppression in vivo via systemic nanoparticle-mediated delivery of PTEN mRNA," were published in *Nature Biomedical Engineering*.

The work was developed by a team of researchers from the Brigham and Women's Hospital (BWH) and Boston Children's Hospital in collaboration with investigators from the Memorial Sloan Kettering Cancer Center.

"The potential impact of this mRNA-based nanotherapeutic is that it offers a new strategy for cancer treatment and can complement currently available therapies such as target inhibitors," Jinjun Shi, PhD, an associate professor of Anesthesia at BWH and study author, said in a press release.

"Loss or mutation of *PTEN* has been observed in about half of metastatic castration-resistant prostate cancers [prostate cancer that keeps on growing even when testosterone levels are low] and in many other human cancers, yet the reconstitution of functional *PTEN* has proven difficult," Shi added.

The Boston-based research team devised a strategy that allows PTEN mRNAs to be reintroduced into prostate cancer cells, working to activate the body's natural response against the tumor. To do so, the scientists developed special nanoparticles that

are able to transport and deliver mRNAs to the cancer cells.

In this preclinical study, investigators were able to show that PTEN mRNA delivered by nanoparticles successfully infiltrated cancer cells cultured in a lab dish, preventing PTEN mRNA degradation and, consequently, restoring the protein's normal tumor-suppressor function, culminating in cancer cell destruction. Restoring tumor suppression also prevented tumor growth and disease progression in multiple mouse models of prostate cancer, including one prone to the development of bone metastases.

Importantly, researchers also demonstrated these nanoparticles are highly stable in blood serum of the mice and were not associated with any toxic side effects.

"This work is the first proof-of-concept of using nanotechnology for systemic delivery of mRNA to restore tumor-growth suppression *in vivo*, including in the metastatic setting where the tumor burden is widely distributed. Our approach may prove useful in treatment of a myriad of malignancies and for other unmet medical needs," said Omid Farokhzad, MD, a study author and director of Center for Nanomedicine at Brigham and Women's Hospital.

These findings demonstrate the anti-cancer potential of PTEN mRNA delivery through nanoparticles, and pave the way for future preclinical studies testing PTEN and other types of tumor-suppressor genes, such as p53, before possibly moving into human clinical trials.

"Because PTEN loss is frequent in late stage PCa [prostate cancer], we suggest that this approach may have feasibility in this patient population," the researchers wrote.

"[C]onsidering the strong potential of mRNA therapy and the lack of systemic studies of *in vivo* mRNA transfection [infiltration] of tumor's, this study sheds light on the useful application of NP [nanoparticle]-mediated mRNA delivery for validating tumor suppressors (for example, PTEN and p53) as therapeutic targets in the treatment of cancer," they added.

Joana Carvalho

Source URL: https://prostatecancernewstoday.com/2018/09/27/pten-protein-restored-using-mrna-and-nanoparticles-in-prostate-cancer-mice-models/

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