Liquid Biopsy Shows Promise in Advanced Prostate Cancer

“Liquid biopsy” analyses of circulating tumor DNA (ctDNA) from blood samples potentially reveal prognostic information about metastatic castration-resistant prostate cancer (mCRPC), and might point the way for development of new targeted treatments, according to findings presented ahead of the 2017 American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium, held February 16–18 in Orlando, Florida.

The study (abstract 149) found that ctDNA was detected in 94% of patients with mCRPC, with genetic alterations similar to those seen in tumor tissue, reported Guru Sonpavde, MD, of the University of Alabama at Birmingham Comprehensive Cancer Center.

“This ctDNA test is now a valuable research tool to discover new molecular targets,” said Sonpavde, in a press release. “Eventually, it may also serve as a noninvasive alternative to the traditional tumor biopsy in cases where tissue biopsy is not safe or feasible. However, we’ll need a controlled, prospective clinical trial to confirm that selecting treatment based on the molecular information from this blood test improves patient outcomes.”

A higher number of overall gene alterations and androgen receptor (AR) gene alterations appeared associated with poor clinical outcomes.

New AR alterations frequently appeared after therapy, the team found—suggesting that liquid biopsies could detect the early stages of acquired drug resistance and provide

(Continued on page 2)
insights for the development of new treatments.

A better understanding of mCRPC biology is needed and will likely require repeated analyses of metastatic tumor biology, Sonpavde said. The disease is currently incurable. Noninvasive serial ctDNA analysis is likely to be less confounded by sampling bias than tumor tissue biopsy, which can underestimate tumors’ genetic heterogeneity.

The research team studied ctDNA from 514 patients with mCRPC using the next-generation sequencing Guardant360 blood test, a 73-cancer-gene panel for cell-free ctDNA. The median age of patients was 71 years (range, 39–91 years); 74% had metastatic bone tumors, which can be difficult to biopsy, and 11.7% of patients had visceral metastases.

Mutations were detected in TP53 (36% of patients), AR (22%), APC (10%), NF1 (9%), EGFR (6%), CTNNB1 (6%), and ARID1A (6%). Gene copy number amplifications were noted for three potentially tumor growth-driving genes: AR (30% of patients), MYC (20%), and BRAF (18%). Clinical outcome data were obtained for 163 of the patients, among whom a higher number of gene alterations was modestly associated with shorter time to treatment failure (TTF; hazard ratio [HR], 1.05; P = .026). AR alterations might also be associated with shorter TTF and survival but these trends had statistically marginal significance (for TTF: HR, 1.42; P = .053; for survival: HR, 2.51; P = .09). Serial testing through time for 64 patients identified evolution of AR, BRCA1, and BRCA2 mutations following treatment.

Patients who had prior therapy for mCRPC had significantly more new alterations in AR (56% vs 37%; P = .028).

While there are not yet agents approved by the US Food and Drug Administration for treating the identified gene alterations in prostate cancer, Sonpavde noted that these findings suggested that salvage therapy agents that target AR mutations might be a particularly promising avenue of research.

“As we work to tailor treatment to the molecular changes driving the growth of cancer in each patient, these blood tests appear very promising, especially for patients who are unable to undergo a tumor biopsy,” said ASCO Expert Sumanta Pal, MD, of City of Hope in Duarte, California, in a press release.

By Bryant Furlow February 13, 2017
ASCO Genitourinary Cancers Symposium, Prostate Cancer
http://www.cancernetwork.com/asco-genitourinary-cancers-symposium/liquid-biopsy-shows-promise-advanced-prostate-cancer

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The quality of life men have after prostate cancer is influenced by the type of treatment they choose, a recent study confirms.

Researchers found that two years out, patients do better in areas like sexual function and urinary incontinence after having certain currently available treatments versus others.

"Prostate cancer is very, very common," said lead author Dr. Gary Chien, who is director of the urology residency program at Kaiser Permanente in Los Angeles. "One out of five men are diagnosed with it in their lifetime. In addition to cancer cure one of the things physicians and patients want to achieve is quality of life."

Chien and colleagues write in BJU International that previous studies examined whether men could be cured and preserve their urinary and sexual function. Many of those studies were not comprehensive and many are out of date, they authors add.

For the new study, the researchers analyzed surveys completed by 5,727 men in the Kaiser Permanente health system who were diagnosed with prostate cancer from March 2011 to January 2014. The men averaged 64 years old.

Participants answered surveys about their quality of life before their treatment and again one, three, six, 12, 18 and 24 months later - until November 2014. The survey asked about urinary incontinence and irritation, sexual function, bowel function and hormone issues.

Overall, 2,389 men had active surveillance, which only monitors the cancer without intervening, 1,861 had their prostates removed with robotic surgery and 828 had the hormone treatment known as androgen-deprivation therapy. Another 309 had external radiation, 199 had their prostates removed with traditional open surgery, 132 had internal radiation and nine had cryoblation, a technique to destroy the tumor by freezing it.

The researchers found that sexual function declined after all treatments, compared to the active surveillance group. Men who had their prostates surgically removed had the greatest decline in function, but it was less severe with the robotic procedure compared to men who had open surgery.

By the end of 24 months, men who had the robotic procedure were on a par in terms of sexual function with men who had either of the two types of radiation treatment.

"Someone who undergoes robotic prostatectomy will likely experience a better sexual function return than open prostatectomy," Chien told Reuters Health.

Urinary incontinence was also worst after surgical prostate removal compared to active surveillance. Of all the treatments, only the hormonal therapy was not associated with worse incontinence compared to active surveillance.

Differences among the other quality of life measures were not as extreme, and the findings are similar to those of past research, the authors note.

Intuit Surgical, maker of robotic surgery equipment, funded the study.

The researchers can't tell whether the differences between treatments in function levels afterward are significant enough to be noticeable to patients, Chien said.

But there are a number of cancer registries around the United States collecting similar data, he added. "Our study shows us a window into what those registries will show."

BJU International, online April 19, 2017
By Andrew M. Seaman
Fri May 5, 2017 Reuters Health
SOURCE: bit.ly/2q8okoZ
www.reuters.com/article/us-health-cancer-prostate-idUSKBN1812AX

"Raising Awareness.....Spreading the Word"

The Manitoba Prostate Cancer Support Group works to increase education, awareness and support for the prostate cancer community. These services are provided through a variety of activities and are available without cost to the existing patient population as well as to the public at large.

Raising awareness is especially important to encourage more men, who may already have prostate cancer but don't yet know about it, to get checked.

Early detection makes all the difference in effecting a cure. As part of our efforts to raise awareness our group provides speakers to community groups, as well as attending "health fairs" in shopping malls and the like.

If your group would like to have a speaker talk about prostate cancer contact board member Pat Feschuk (Special Events organizer; telephone 204-654-3898; or email at lizpat@shaw.ca) to make arrangements.
Don't Hesitate to Watch Prostate Cancer in Young Men

BOSTON — Active surveillance is a safe and effective treatment option for young men (<60 years) with low-risk prostate cancer, according to a new cohort study presented here at the American Urological Association (AUA) 2017 Annual Meeting.

However, judging by comments made at the meeting, that message may be hard to hear and accept, even at academic medical centers.

Men younger than 60 years have outcomes that are "comparable" to those reported in the literature for older men, said lead study author Keyan Salari, MD, chief resident in urologic surgery at Massachusetts General Hospital (MGH) in Boston.

The new study involved 432 young men with low-risk disease who were managed with surveillance between 1990 and 2016 at MGH (n = 181) and Sunnybrook Health Sciences Center in Toronto, Ontario, Canada (n = 251).

Metastasis-free survival was 99.7% and 97.5% at 5 and 10 years, respectively.

Five patients developed metastasis (two with positive lymph nodes at time of radical prostatectomy, three with distant metastasis). There were no prostate-cancer specific deaths. The median follow-up was 5.1 years.

Typically, men of this younger age are counseled into treatment, said Dr Salari. That is because of their longer life expectancy, fewer comorbidities (compared with older men), and perceived likelihood of eventually needing definitive treatment.

There also have not been many data to indicate that watching these younger men was okay.

However, the new retrospective data provide evidence that it is more than okay, suggested Dr Salari.

There is "no need for hesitancy," he said, adding that men younger than 60 years "shouldn't be excluded" from active surveillance. The criteria for active surveillance are "expanding," he commented.

But there is, and has been, hesitancy about including younger men, even at a pioneering active surveillance center like MGH, said another coauthor.

"The data for younger men are especially important. Even some of our colleagues at MGH are hesitant to place younger men on active surveillance," said Adam Feldman, MD, a urologist at MGH who also attended the news conference and spoke up from the audience.

The new data include the estimation that 74.3% of the men were free from treatment at 5 years, and 55.4% at 10 years.

"This is very compelling for young men who at least want to delay radical treatment for a period of years," said Stacy Loeb, MD, a urologist at New York University in New York City, who acted as the news conference moderator.

It is a durable option, with very few men developing metastases and more than half free from treatment at 10 years, she summarized.

In Sweden, among men 50 to 59 years old, 88% of very low risk patients and 68% of low-risk patients were managed with active surveillance in 2014, Dr Loeb also pointed out. "It really is possible for young men to do this," she said.

Who Is Likely to Progress to Treatment

In a 432-patient study population, the median prostate-specific antigen (PSA) level was 4.6 ng/mL, with only 11 of the men having PSA levels of 10 ng/mL or higher. Almost all the patients had Gleason 6 or lower (97.7%) and clinical stage T1 (91.9%) disease.

Dr Salari reported that 84.3% of the men had a repeat biopsy, with 62.6% showing prostate cancer, 24.5% benign, 7.7% with prostatic intraepithelial neoplasia, and 5.2% with atypia. The high proportion of benign follow-up biopsies were a result of sampling errors that are to be expected because of the imprecision of ultrasound-guided biopsies and the presence of so many low-volume tumors, said Dr Salari.

Over time, 131 men (30.3%) progressed to treatment for the following reasons: pathologic progression (64.1%), PSA progression (18.3%), patient preference (11.5%), volume progression (3.1%), and other reasons (3.1%).

Dr Salari said there were only two predictors of progression to treatment,

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and both conferred about a doubling of risk compared with patients who did have the measures.

Namely, patients who had more than 20% tumor tissue in any one biopsy core (compared with those with 20% or less in all of their cores) were nearly twice as likely to move onto treatment (hazard ratio, 1.87; P = .0016), as were patients with PSA density of 0.15 or higher (compared with those with less; hazard ratio, 1.98; P = .01).

Among the 131 treated patients, 62.6% underwent radical prostatectomy, 13.0% underwent high-intensity focal ultrasound therapy, 12.2% underwent external beam radiation, and 10.7% had brachytherapy.

Among the surgery patients, pathologic review after surgery showed that 88.2% (60/68) were pT2, and 11.8% (8/68) were pT3.

Active surveillance of men younger than 60 years "spares most men from intervention," and allows "adequate time" for intervention for most, concluded Dr Salari.


dr salari and dr feldman have disclosed no relevant financial relationships. dr loeb has disclosed financial relationships with mdx health, armune bioscience, minomic, boehringer ingelheim, genomedx biosciences, and astellas.


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New 'Magic Bullet' Prostate Cancer Therapy Delivers Promising Results

By Gabriella Rogers

Australian doctors are witnessing promising results of a new therapy for men with prostate cancer who've tried everything to stop their disease from spreading.

The treatment, known as theranostics, offers a more targeted way of mapping and killing cancer cells.

Pivotal to the emerging science is the German discovery of small molecules that are able to latch onto the surface of prostate cancer cells called prostate-specific membrane antigen (PSMA) receptors.

"I call it a tsunami of change for prostate cancer," Associate Professor Louise Emmett, a nuclear medicine specialist at Sydney's St Vincent's Public Hospital, said.

"It has completely changed the way we diagnose prostate cancer in a lot of men and now it's changing the way we treat them at this very end stage of the disease."

Boris Kogan, 76, exhausted all treatments, including chemotherapy, after the disease spread to his liver and lungs.

Mr Kogan was eligible for the trial and received injections of a radioactive agent called Lutetium 177, which is bound to a PSMA molecule. This allows it to seek and destroy prostate tumours.

Highly specific PET imaging then gives doctors a birds-eye view of the results.

Mr Kogan's son-in-law Arthur said the tumours were "disappearing in front of our eyes, it was like science fiction".

Doctors are equally impressed by the results.

"It's like a magic bullet," Dr Emmett said.

"It goes for the target and it stays there, concentrates there and kills those cells.

"Half of the men who get this treatment have a very good response."

St Vincent's Hospital in Sydney and Melbourne's Peter MacCallum Cancer Centre are collaborating on trials for the new therapy.

Dr Emmett and her colleagues recently published a review of the current evidence in the Journal of Medical Radiation Sciences.

She said a third of patients on the therapy will get a dry mouth, while some experience nausea.

Mr Kogan said he experienced no issues with the treatment, compared to the gruelling side-effects of chemotherapy.

Prostate cancer is the most commonly diagnosed cancer among men in the western world and it accounts for about 25 percent of all new male cancer cases in Australia.

Dr Emmett said the future of theranostics was bright and she was confident the technology could be used on patients with other cancers.

"We'd definitely be moving with this technology into other cancers, once we find the appropriate receptor," Dr Emmett said.

May 18, 2017


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Cancer Diagnosis: 11 Tips For Coping

If you've been diagnosed with cancer, knowing what to expect and making plans for how to proceed can help make this stressful time easier.

Learning that you have cancer is a difficult experience. After your cancer diagnosis, you may feel anxious, afraid or overwhelmed and wonder how you can cope during the days ahead. Here are 11 suggestions for coping with a cancer diagnosis.

Get the facts about your cancer diagnosis

Try to obtain as much basic, useful information about your cancer diagnosis as you need in order to make decisions about your care.

Write down your questions and concerns beforehand and bring them with you. Consider asking:

♦ What kind of cancer do I have?
♦ Where is the cancer?
♦ Has it spread?
♦ Can my cancer be treated?
♦ What is the chance that my cancer can be cured?
♦ What other tests or procedures do I need?
♦ What are my treatment options?
♦ How will the treatment benefit me?
♦ What can I expect during treatment?
♦ What are the side effects of the treatment?
♦ When should I call the doctor?
♦ What can I do to prevent my cancer from recurring?
♦ How likely are my children or other family members to get cancer?

Consider bringing a family member or friend with you to your first few doctor appointments to help you remember what you hear.

You might also want to consider how much you want to know about your cancer. Some people want all the facts and details, so they can be very involved in the decision-making process. Others prefer to learn the basics and leave details and decisions to their doctors. Think about which approach works best for you. Let your health care team know what you’d prefer.

Keep the lines of communication open

Maintain honest, two-way communication with your loved ones, doctors and others after your cancer diagnosis. You may feel particularly isolated if people try to protect you from bad news or if you try to put up a strong front. If you and others express emotions honestly, you can all gain strength from each other.

Anticipate possible physical changes

Now — after your cancer diagnosis and before you begin treatment — is the best time to plan for changes. Prepare yourself now so that you’ll be better able to cope later.

Ask your doctor what changes you should anticipate. If drugs will cause hair loss, advice from image experts about clothing, makeup, wigs and hairpieces may help you feel more comfortable and attractive. Insurance often helps pay for wigs, prostheses and other adaptive devices.

Members of cancer support groups may be particularly helpful in this area and can provide tips that have helped them and others.

Also consider how treatment will impact your daily activities. Ask your doctor whether you can expect to continue your normal routine. You may need to spend time in the hospital or have frequent medical appointments. If your treatment will require a leave of absence from your normal duties, make arrangements for this.

Maintain a healthy lifestyle

This can improve your energy level. Choose a healthy diet consisting of a variety of foods and get adequate rest in order to help you manage the stress and fatigue of the cancer and its treatment.

Exercise and participating in enjoyable activities also may help. Recent data suggest that people who maintain some physical exercise during treatment not only cope better but may also live longer.

Let friends and family help you

Often friends and family can run errands, provide transportation, prepare meals and help you with household chores. Learn to accept

(Continued on page 7)
their help. Accepting help gives those who care about you a sense of making a contribution at a difficult time.

Also encourage your family to accept help if it's needed. A cancer diagnosis affects the entire family and adds stress, especially to the primary caregivers. Accepting help with meals or chores from neighbors or friends can go a long way in preventing caregiver burnout.

Review your goals and priorities

Determine what's really important in your life. Find time for the activities that are most important to you and give you the most meaning.

If needed, try to find a new openness with loved ones. Share your thoughts and feelings with them. Cancer affects all of your relationships. Communication can help reduce the anxiety and fear that cancer can cause.

Try to maintain your normal lifestyle

Maintain your normal lifestyle, but be open to modifying it as necessary. Take one day at a time. It's easy to overlook this simple strategy during stressful times. When the future is uncertain, organizing and planning may suddenly seem overwhelming.

Consider how your diagnosis will impact your finances

Many unexpected financial burdens can arise as a result of a cancer diagnosis. Your treatment may require time away from work or an extended time away from home. Consider the additional costs of medications, medical devices, traveling for treatment and parking fees at the hospital.

Many clinics and hospitals keep lists of resources to help you financially during and after your cancer treatment. Talk with your health care team about your options.

Talk to other people with cancer

Sometimes it will feel as if people who haven't experienced a cancer diagnosis can't fully understand how you're feeling. It may help to talk to people who have been in your situation. Other cancer survivors can share their experiences and give you insight into what you can expect during treatment. You may have a friend or family member who has had cancer. Or you can connect with other cancer survivors through support groups. Ask your doctor about support groups in your area or contact your local chapter of the American Cancer Society. Online message boards also bring cancer survivors together. Start with the American Cancer Society's Cancer Survivors Network.

Fight stigmas

Some old stigmas associated with cancer still exist. Your friends may wonder if your cancer is contagious. Co-workers may doubt you're healthy enough to do your job, and some may withdraw for fear of saying the wrong thing. Many people will have questions and concerns.

Determine how you'll deal with others' behaviors toward you. By and large, others will take their cues from you. Remind friends that even if cancer has been a frightening part of your life, it shouldn't make them afraid to be around you.

Develop your own coping strategy

Just as each person's cancer treatment is individualized, so is the coping strategy you use. Ideas to try:

- Practice relaxation techniques.
- Share your feelings honestly with family, friends, a spiritual adviser or a counselor.
- Keep a journal to help organize your thoughts.
- When faced with a difficult decision, list the pros and cons for each choice.
- Find a source of spiritual support.
- Set aside time to be alone.
- Remain involved with work and leisure activities as much as you can.

What comforted you through rough times before your cancer diagnosis is likely to help ease your worries now, whether that's a close friend, religious leader or a favorite activity that recharges you. Turn to these comforts now, but also be open to trying new coping strategies.

By Mayo Clinic Staff

References


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2017 MEETINGS

Jul-20  Panel discussion
- Promoting patient self-help in dealing with prostate cancer
- Gayle Nichols (resource), Pamela Klassen (diet), Jennifer McLaren (exercise)

Aug-17  Dr. Spencer Gibson - Manitoba Institute for Cell Biology
- Genetic research approaches to improved therapy

All meetings (except September) will be held at:
Cindy Klassen Recreation Complex at 999 Sargent Avenue

All meetings are 7 – 9 pm.
Everyone Welcome

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