Informed Prostate Cancer Support Group Inc.
"A 501 C 3 CORPORATION ID # 54-2141691"

MAY 2022 NEWSLETTER

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Wednesday, May 18, 2022

Volume 15 Issue 05

- **Next Meeting Saturday, May 21, 2022 IPCSG - Live-Stream Event, 10:00am PT**.
- Immunotherapy -Dr. Tanya Dorff is a medical oncologist who serves as associate clinical professor in the Department of Medical Oncology & Therapeutics Research and the Head of the Genitourinary Cancers Program at City of Hope, a research and treatment center for cancer based in Duarte, California.. Dr. Dorff's research interests in prostate cancer range from clinical trials in PSA-recurrent prostate cancer to the role of fasting in chemotherapy tolerability to CAR T cells that are primed to target prostate cancer tissue...
- Due to COVID-19, no in-person meetings at the Sanford Burnham Prebys Medical Discovery Institute will take place until further notice. This meeting will be live-streamed and will also be available on DVD.
- **For further Reading: https://ipcsg.blogspot.com/**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org
- **If you would like some copies of our new brochure by mail for distribution to your friends or physicians, please send email to lewis.bill@gmail.com or call Bill at 619-370-8789**

April 2022 Informed Prostate Cancer Support Group Meeting

Summary by Bill Lewis

Advanced Prostate Cancer
Richard Lam, MD, Prostate Oncology Specialists, Marina del Rey, CA

Abstract: A double board-certified internist and oncologist, Richard Lam, MD, has been specializing full time at Prostate Oncology Specialists in the treatment of prostate cancer since 2001. Dr. Lam will be discussing the latest news about Metastatic Prostate Cancer, treatments and clinical trials.

Types of Metastatic Cancer - where are the metastatic tumors? What's the prognosis?

Regional lymph nodes: up to 15 years (or cure).
Bone only: 2-10 years (depends on number and location).
Organ (visceral) involvement: Liver and Lungs (2-3 years, but up to 10 years for lung disease).
Oligometastatic disease: many years or even possible cure.

Imaging tests used to detect metastases:

CT Scan (computed tomography) – rarely used nowadays. Not ideal for soft tissue lesions.
MRI Scan magnetic resonance imaging – also better for bones rather than soft tissues.
Nuclear scans
T-99 bone scan – an old standard for examining bones for metastases.
C-11 PET choline/acetate scan – more sensitive test, but limited availability.

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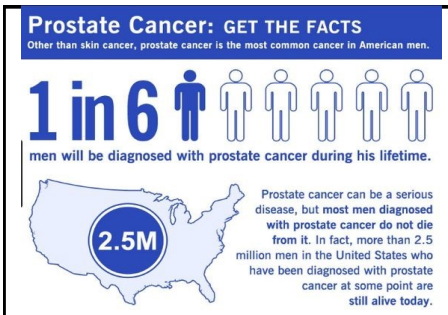

Organization

a 501c3 non-profit organization - all positions are performed gratis

IPCSG

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NEWSLETTER
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PROSTATE CANCER—*2 WORDS, NOT A SENTENCE*

What We Are About

Our Group offers the complete spectrum of information on prevention and treatment. We provide a forum where you can get all your questions answered in one place by men that have lived through the experience. Prostate cancer is very personal. Our goal is to make you more aware of your options before you begin a treatment that has serious side effects that were not properly explained. Impotence, incontinence, and a high rate of recurrence are very common side effects and may be for life. Men who are newly diagnosed with PCa are often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

Meeting Video DVD's

DVD's of our meetings are available for purchase on our website at https://ipcsg.org/purchase-dvds and are generally available by the next meeting date.

Join the IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up and HELP. Call **President** Bill Lewis @ (619) 591-8670 ; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

Due to COVID-19, no in-person meetings will be held until further notice. We will continue to post and distribute the newsletter in the interim. Our speaker this month will be broadcast via the IPCSG website at https://ipcsg.org/live-stream and can be watched by scrolling down and clicking on the "WATCH THE PRESENTATION" button. The broadcast will begin approximately 10 minutes before to the listed start time.

In this issue:

Bill Lewis produced a summary of the last stream video, .

Articles of Interest:

1. Is Ivermectin a Cancer Solution? - *can inhibit growth of PCa cells*
2. Most Men With Low-Risk Prostate Tumors Now Forgoing Treatment *60% of eligible now on AS*
3. Yes, Nodal Recurrence of Prostate Cancer is Potentially Curable - *trial shows radiotherapy can cure in some cases*
4. The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial-
5. Benefits of PSA prostate cancer screening found to be more favorable than previous estimates, especially for blacks- *new analysis supports PSA screening, particularly for Black men and others at high risk*

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Axumin PET scan – comparable sensitivity, and widely available.
PSMA PET scan – more sensitive, and has become the new go-to test for metastases.
Ga-68 (available at UCLA and UCSF)
F-18 PYL ("Pylarify"; increasingly wide availability and popularity – at least 15 centers in the San Diego area already offer it)

These PSMA PET scans are now not only given when there is relapse after treatment, but also to verify that there are no metastases already present before initial treatment (e.g., before choosing surgery, radiation, or focal therapy).

Ways to differentiate aggressive vs. non-aggresive metastatic PCa: Gleason score, PSA level, Number of spots, Location (visceral vs bone), and Genetic testing (Germline and/or Somatic – see Dr. Lam's lecture in November 2020, summarized in the December newsletter).

Regional Lymph Node Involvement may be curable. After Prostatectomy with Extended Lymph Node Dissection +/- Radiation +/- Androgen Deprivation Therapy (ADT), about 20% of men have an extended period of remission. When ADT is included, about half of these men will have extended remission. If there is only one node diseased, the remission may last longer than four years.

Recently, without doing surgery, excellent results for such disease have been achieved using radiation to the prostate and pelvic region + ADT (18-36 months) + 2nd Gen AR (Zytiga, Xtandi, or the like). This approach avoids the likelihood of incontinence and/or erectile dysfunction due to surgery.

Is Oligometastatic Disease Curable? Defined as <5 lesions (Optimally <3), including not in nearby lymph nodes. Delay in relapse, delay to CRPC (castrate resistance) and long term (4-5 years) remissions have been reported. Treat the prostate and treat the oligo-mets with surgery (in case of nearby lymph nodes), SBRT (highly focused radiation) or pelvic region radiation. It is helpful to add systemic therapy w/ ADT + 2nd generation androgen receptor inhibitor.

Metastatic Disease is Usually Managed as a Chronic Condition. Medications are used to shrink the tumors, and prevent growth, thus prolonging survival for years. Radiation is used to treat symptoms and may delay the need for ADT (STOMP Trial). "Liquid Radiation" (Xofigo) can prolong survival.

What is ADT? Androgen Deprivation Therapy is a pharmaceutical method for cutting the amount and/or binding of testosterone to prostate (cancer) cells. The androgen (testosterone) promotes prostate cancer cell growth. ADT causes programmed cell-death. Androgens are 90% produced in the testicles, and 10% in the adrenal glands. See the December 2019 newsletter for a talk by Dr. Lam that focused on ADT.

Various drugs, including Lupron, are "agonists" and overstimulate the production of testosterone, causing its production to crash and stop. Firmagon (degarelix; monthly injection) is an antagonist and stops testosterone production more quickly (and has less chance of cardiovascular side effects). About a year ago, Orgovyx (relugolix) was introduced as a daily oral pill, and it acts very quickly, both to lower testosterone and to allow its return when the drug is stopped. Both these antagonists do not produce a flare of testosterone (vs. Lupron), so Casodex (bicalutamide) at the start of treatment is not needed. They can quickly reduce tumors compressing the spine or the ureter, for relief of pain/paralysis or urination difficulties. Orgovyx is not yet covered by all insurance plans. Firmagon injections can be painful [but injecting deep instead of just "subcutaneous" and leaving the needle inserted for a minute or two after the injection nearly eliminates the pain and swelling, per Bill Lewis' experience.]

All the ADT drugs can have side effects due to the low testosterone. Refer to the December 2019 newsletter.

In 2015, it was shown that adding docetaxel (Taxotere) chemotherapy to ADT improved survival by about a year.

Improvements on ADT-alone have also been observed by adding "second generation" Androgen Receptor Inhibitor drugs, which now include Abiraterone (Zytiga, usually taken with Prednisone), Enzalutamide (Xtandi), Apalutamide (Erleada), and Darolutamide (Nubeqa). Initially, these drugs were added when ADT stopped working. Since 2017, it has been shown that they give greater benefit (comparable to chemotherapy) for newly diagnosed metastatic patients, still "castrate sensitive," where ADT shrinks tumors. And in the past year, it has been shown

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that it is even better to combine ADT + chemotherapy + abiraterone or darolutamide "up front."

For castrate resistant metastatic PCa (tumor growth is no longer prevented by ADT drugs, the PSA goes up, and new spots appear), if not already used, the drugs mentioned above may be added to the no-longer-effective ADT. For patients with a DNA repair genetic defect – about one-third of patients – a PARP inhibitor such as Lynparza (Olaparib) can be useful. Again, see the genetic testing lecture summarized in the December 2020 newsletter.

Radiation to the pelvis or to single spots has often been used against metastases. "Liquid radiation" to bone-only metastases anywhere in the body can be given using Radium-223 (Xofigo). Injected Lutetium-177, FDA-approved in March, treats PCa in any tissue, not just bone mets, if the cancer expresses the PSMA protein. It decreases symptoms and gives remission for months to over a year. Side effects are less than for chemotherapy.

Immunotherapy may also be useful. Dr. Tanya Dorff will focus on this topic next month. Provenge has been used for about ten years, mainly for patients with low volume, low aggressive metastatic castrate resistant PCa. Pembrolizumab (Keytruda) is used against cancers, including PCa, with microsatellite instability (high tumor mutation burden). About one in 20 men have such mutations. Ipilimumab + Nivolumab gives a good response in about one of 5 men.

Bone Protective Agents decrease bone loss, bone pain and fracture risk, and include zoledronic acid (Zometa) and denosumab (Xgeva or Prolia).

New developments: Actinium (Ac-225) is a second-generation liquid radiation. It seems to give fewer side effects vs. Lutetium-177. HPN-424 therapy combines immunotherapy + PSMA targeted liquid radiation. Newer PARP inhibitors include Rucaparib, Niraparib, and Talazoparib. The combination of a PARP inhibitor (Olaparib) + abiraterone for metastatic castrate resistant PCa gives a benefit even in men who do not have an identified DNA repair genetic defect. Cool!

Conclusion: "Lots of reasons to be optimistic."

Questions:

What patients are suitable to be treated with Lutetium-177? Those with metastatic castrate resistant PCa, who have been treated with Taxotere chemotherapy. It's still not approved to be used in earlier stages (as has always been the case with new drugs). But the needed studies are underway. Another factor is that Dr. Lam would prefer to reserve it for when there are many metastases, since oligometastatic disease may probably be treatable with SBRT (focused radiation). Repeated treatments with Lutetium-177 may not be advisable, due to damaging the bone marrow – but it's being studied.

What about estrogen patches to add back a physiologic level of estradiol while on Zytiga, since studies suggest that estradiol is not worse than ADT for cardiovascular problems? Using estrogen is a multi-edged sword. Just as for women, it does help prevent bone loss, decrease hot flashes and improve overall quality of life. But it can cause breast enlargement, and the oral form is known to cause blood clots in the lungs, heart attacks and strokes. But Dr. Lam does sometimes prescribe patches, at the lowest possible dose, because he believes the risk of blood clots, etc. is very low. Because metastatic PCa itself causes an increase in the risk of cardiovascular problems, adding estrogen – even via patches – should be weighed carefully. There used to be a protocol involving high doses of estrogen to fight PCa, and about one in four patients responded well.

What about BAT (bipolar androgen therapy)? This is use of high dose testosterone for men who are castrate resistant. About one out of six of these men had a transient response. But there was a lot higher risk of heart attacks and strokes. Dr. Lam prefers other newly developed protocols, is waiting for more data, and would consider this a desperation choice at this time.

Is continuing Lupron while on Zytiga useless, as one member's oncologist declared? There is a growing opinion toward this, but more long-term data is needed. This member reports a rising PSA and testosterone, a year since he was taken off Lupron. Dr. Lam would encourage him to take Firmagon or Orgovyx in addition to continuing Zytiga, to (quickly) push the testosterone back down, or he could just go back on Lupron.

How has the pandemic affected Prostate Oncology Specialists? Dr. Scholz was not able to continue employing Dr. Turner, and asked Dr. Lam to work part-time. They've stopped taking some insurances (poor reimbursements

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and too much paperwork) and now have a "membership/concierge" business model. They are able to do virtual video meetings and get reasonable reimbursement. They get no payment for phone consultations. Overall, they are doing OK.

A 78-year-old member asked about treatments after 3 years of active surveillance. A recent PSMA test indicated that there are no metastases. It would depend on any other illnesses he has, urinary & sexual issues, and quality of life considerations. Dr. Lam would suggest radiation if he wants treatment. UCLA can do focal radiation and only treat half the prostate – with half the side effects. Medication is also an option, such as low-dose Casodex or intermittent Lupron, which might contain the cancer for 10-20 years.

What about single doses of Lutetium-177 being given in Germany for hormone-sensitive PCa? He would be reluctant for such patients, who are likely to live a long time, because of unknown long-term effects. However, for castrate resistant PCa, one or two doses of Lu-177 before chemotherapy is being looked at.

A member has rising PSA on Zytiga. What next? Any of the "lutamides" -- Enzalutamide (Xtandi), Apalutamide (Erleada), or Darolutamide (Nubeqa) may be helpful, but he should get an ar-v7 genetic test first, because if it is positive, these drugs will not work. Then he may want to consider chemotherapy or liquid radiation, depending on what his scans show.

A member just started Orgovyx and Nubeqa, having three metastatic spots in his pelvic area. He probably does not need chemotherapy, and if given radiation to the spots, may achieve 5-7 years of remission.

What PSA level is needed on recurrence after surgery, for good sensitivity in scans, including PSMA-PET scans? Dr. Lam noted that whereas it used to be recommended that radiation be given soon after surgery, now it has been found that it is usually OK to wait until the PSA rises a bit. It allows the patient to more fully recover. At PSA = 0.2 (or sometimes at 0.15), radiation is then given. Even if the PSMA scan at PSA = 0.2 is negative, Dr. Lam would still want to seriously discuss irradiating the prostate bed, rather than waiting for PSA = 0.3 or 0.4. A PSMA scan is usually "good" at PSA = 0.2, and can sometimes be useful even at PSA = 0.1.

What about considerations of the testosterone level in recurrence? If the testosterone level were low, say 80 (not at fully castrate level), he would take action sooner on a rising PSA than if the testosterone level were closer to normal – say 200 or 300, since the cancer is obviously growing without needing "normal" testosterone.

What about ADT holidays to delay castrate resistance? It has been shown that holidays generally neither delay nor speed up castrate resistance. Of course, on holidays, one avoids the side effects of continuous treatment, resulting in better quality of life. However, with metastatic PCa, especially if there are many tumors, holidays CAN speed up castrate resistance, so should be avoided. But Dr. Lam considers that it's OK to take holidays with oligometastatic PCa.

Is constant exercise helpful in tolerating and reducing the side effects of treatment? 100% yes. Both cardio and weight training help prevent muscle and bone loss, helping keep you strong through successive treatment protocols.

What about using metformin during treatment? Isn't exercise more useful? It's like a cherry on top. Its main effect is likely to be avoidance of weight gain.

What other signs of increasing disease beside PSA are there, that one might feel or sense? You are very unlikely to feel symptoms until the PSA is above 10. It's very highly correlated with disease growth and tumor burden. There is one exception. Neuroendocrine dediffentiated metastatic disease produces little or no PSA. It's hard to diagnose, hard to treat, and fortunately is very rare. ADT doesn't help very long, so one turns to chemotherapy and PARP inhibitors.

Note: expect to hear from Dr. Lam again in about a year, not in November, as he prefers this time of year.

See the video online for the talk and slides: https://www.youtube.com/watch?v=oXTSdVk4LkU

A dvd of Dr. Lam's talk and slides will be available for purchase from the IPCSG by the time of next month's meeting. Order online from the IPCSG.org website.

Is Ivermectin a Cancer Solution?

Is Ivermectin a Cancer Solution?
theepochtimes.com
Joseph Mercola

Ivermectin is a widely used antiparasitic drug that's listed on the World Health Organization's essential medicines list[1] and approved by the U.S. Food and Drug Administration. In low- and middle-income countries, ivermectin is commonly used to treat parasitic diseases including onchocerciasis (river blindness), strongyloidiasis and other diseases caused by soil-transmitted helminthiasis, or parasitic worms.[2]

The drug is also used to treat scabies and lice. It's estimated that the total number of ivermectin doses distributed is equal to one-third of the world's population and, as such, "ivermectin at the usual doses (0.2–0.4 mg/kg) is considered extremely safe for use in humans."[3]

Ivermectin also has demonstrated antiviral and anti-inflammatory properties and made headlines for its potential role in treating COVID-19[4] — although much of the positive press has been censored and falsely labeled misinformation.[5] Now researchers are highlighting another potential use for ivermectin, which is equally as exciting as its potential role in COVID-19 — as an anticancer agent.

Ivermectin's Powerful Antitumor Effects

Ivermectin has notable antitumor effects, which include inhibiting proliferation, metastasis and angiogenic activity in cancer cells.[6] It appears to inhibit tumor cells by regulating multiple signaling pathways, which researchers explained in the Pharmacological Research journal, "suggests that ivermectin may be an anticancer drug with great potential."[7]

Their graphic, below, shows the multiple ways that ivermectin may target cancer, including inducing apoptosis and autophagy while also inhibiting tumor stem cells and reversing multidrug resistance. They stated that ivermectin "exerts the optimal effect when used in combination with other chemotherapy drugs."[8]

Many may not be aware that scientists Satoshi ōmura and William C. Campbell won the Nobel Prize in Physiology or Medicine in 2015 for their discovery of ivermectin.[9] The medicine is used to treat not only parasitic diseases like malaria but also shows promise for treating asthma and neurological diseases, in addition to cancer.

Along with direct cytotoxic effects, it's believed that ivermectin regulates the tumor microenvironment, mediating immunogenic cell death — another reason for its promise as an anticancer agent.[10] Research suggests the drug may be useful for *many* cancers:[11]

> **Urinary system cancer** — Ivermectin significantly inhibited the proliferation of five renal (kidney) cell carcinoma lines without affecting normal kidney cells. It also had an inhibitory effect on prostate cancer cells.

Most Men With Low-Risk Prostate Tumors Now Forgoing Treatment

medscape.com
Howard Wolinsky

The number of men with prostate cancer who opted for active surveillance (AS) doubled nationally between 2014 and 2021, according to experts who say the dramatic increase reflects a growing understanding among both researchers and patients that low-grade prostate tumors can be safely watched for years without requiring treatment.

Dr Matthew Cooperberg

Roughly 60% of men eligible for AS chose that approach in 2021, up from 27% in 2014 and less than 10% in 2010, according to panel member Matthew Cooperberg, MD, MPH, of University of California San Francisco. He presented the data for a panel of the American Urological Association (AUA) today at the group's 2022 annual meeting in New Orleans.

Cooperberg attributed the hike in AS rates in the United States to the growing scientific literature and guidelines supportive of the approach, which calls for periodic assessments of low-risk tumors but no surgery, radiation, or other therapies. In Canada and parts of Europe, approximately 80%-90% of men who are eligible for AS choose that approach, experts said.

Earlier this month, the AUA and the American Society for Radiation Oncology released the strongest guidelines to date supporting AS for low-risk patients, and, for the first time, for select patients with favorable intermediate-risk prostate cancer.

In 2012, the US Preventative Services Task Force (USPSTF) recommended against screening for prostate-specific antigen (PSA), concluding that the benefits of the test did not outweigh the risks, such as overdiagnosis and overtreatment of low-risk prostate cancer.

Urologists blamed the USPSTF policy for a decline in PSA screening and an uptick in the diagnosis of advanced prostate cancer.

Cooperberg said the shift served as "a bit of a wake-up call for at least a segment of the urology community that if we didn't fix the overtreatment problem, we would never retake the chunks of the conversation about screening and early detection."

In 2018, following protests by urologists and patient advocates, the USPSTF revised its statements to include shared decision-making for PSA testing in men aged 55-69 years, reflecting emerging evidence of longer-term benefits and widespread adoption of active surveillance after detection of low-risk disease, he said

Laurence Klotz, MD, the University of Toronto researcher who named and helped develop AS 30 years ago, and who was not on the AUA panel, said other factors also help to explain the growing interest in AS. These include an increasing consensus among experts on the value of the strategy, mounting public awareness of its benefits, the efforts of support and advocacy groups, and the arrival of more sophisticated imaging and biomarkers that help further refine risk.

"We're shrinking the gray zone," Klotz said. "Remaining resistance to AS is due to legitimate concerns about missing significant cancer and losing a patient to metastatic disease, and perhaps financial drivers, particularly with less invasive technologies like radiation and focal therapy."

redjournal.org

Yes, Nodal Recurrence of Prostate Cancer is Potentially Curable

Advances in positron emission tomography (PET) imaging with prostate-specific tracers allow more sensitive and specific detection of low-volume recurrences that were previously indiscernible using conventional imaging. Retrospective data in patients presenting with N1M0 prostate cancer support combined-modality therapy with radiation and androgen deprivation therapy, and preliminary data from the Radiation Therapy Oncology Group 0534 randomized trial suggest that salvage pelvic nodal radiation therapy with androgen deprivation therapy is safe and effective for patients with biochemical recurrence after prostatectomy.

Short term androgen deprivation therapy without or with pelvic lymph node treatment added to prostate bed only salvage radiotherapy: The NRG Oncology/RTOG 0534 SPPORT trial.

A proportion of patients enrolled on Radiation Therapy Oncology Group 0534 would likely have had PET-detected nodal metastases, if PET imaging had been available. It is reasonable to extrapolate that salvage pelvic radiation therapy would be effective in a patient whose primary tumor has been controlled with prior prostate radiation therapy.

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The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial

thelancet.com

Summary

Background

In men with a detectable prostate-specific antigen (PSA) level after prostatectomy for prostate cancer, salvage prostate bed radiotherapy (PBRT) results in about 70% of patients being free of progression at 5 years. A three-group randomised trial was designed to determine whether incremental gains in patient outcomes can be achieved by adding either 4–6 months of short-term androgen deprivation therapy (ADT) to PBRT, or both short-term ADT and pelvic lymph node radiotherapy (PLNRT) to PBRT.

Methods

The international, multicentre, randomised, controlled SPPORT trial was done at 283 radiation oncology cancer treatment centres in the USA, Canada, and Israel. Eligible patients (aged ≥18 years) were those who after prostatectomy for adenocarcinoma of the prostate had a persistently detectable or an initially undetectable and rising PSA of between 0·1 and 2·0 ng/mL. Patients with and without lymphadenectomy (N0/Nx) were eligible if there was no clinical or pathological evidence of lymph node involvement. Other eligibility criteria included pT2 or pT3 disease, prostatectomy Gleason score of 9 or less, and a Zubrod performance status of 0–1. Eligible patients were randomly assigned to receive PBRT alone at a dose of 64·8–70·2 Gy at 1·8 Gy per fraction daily (group 1), PBRT plus short-term ADT (group 2), or PLNRT (45 Gy at 1·8 Gy per fraction, and then a volume reduction made to the planning target volume for the remaining 19·8–25·2 Gy) plus PBRT plus short-term ADT (group 3). The primary endpoint was freedom from progression, in which progression was defined as biochemical failure according to the Phoenix definition (PSA ≥2 ng/mL over the nadir PSA), clinical failure (local, regional, or distant), or death from any cause. A planned interim analysis of 1191 patents with minimum potential follow-up time of 5 years applied a Haybittle-Peto boundary of p<0·001 (one sided) for comparison of 5-year freedom from progression rates between the treatment groups. This trial is registered with ClinicalTrials.gov, NCT00567580. The primary objectives of the trial have been completed, although long-term follow-up is continuing.

Findings

Between March 31, 2008, and March 30, 2015, 1792 eligible patients were enrolled and randomly assigned to the three treatment groups (592 to group 1 [PBRT alone], 602 to group 2 [PBRT plus short-term ADT], and 598 to group 3 [PLNRT plus PBRT plus short-term ADT]). 76 patients subsequently found to be ineligible were excluded from the analyses; thus, the evaluable patient population comprised 1716 patients. At the interim analysis (n=1191 patients; data cutoff May 23, 2018), the Haybittle-Peto boundary for 5-year freedom from progression was exceeded when group 1 was compared with group 3 (difference 17·9%, SE 2·9%; p<0·0001). The difference between groups 2 and 3 did not exceed the boundary (p=0·0063). With additional follow-up beyond the interim analysis (the final planned analysis; data cutoff May 26, 2021), at a median follow-up among survivors of 8·2 years (IQR 6·6–9·4), the 5-year freedom from progression rates in all 1716 eligible patients were 70·9% (95% CI 67·0–74·9) in group 1, 81·3% (78·0–84·6) in group 2, and 87·4% (84·7–90·2) in group 3. Per protocol criteria, freedom from pro-

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gression in group 3 was superior to groups 1 and 2. Acute (≤3 months after radiotherapy) grade 2 or worse adverse events were significantly more common in group 3 (246 [44%] of 563 patients) than in group 2 (201 [36%] of 563; p=0·0034), which, in turn, were more common than in group 1 (98 [18%] of 547; p<0·0001). Similar findings were observed for grade 3 or worse adverse events. However, late toxicity (>3 months after radiotherapy) did not differ significantly between the groups, apart from more late grade 2 or worse blood or bone marrow events in group 3 versus group 2 (one-sided p=0·0060) attributable to the addition of PLNRT in this group.

Interpretation

The results of this randomised trial establish the benefit of adding short-term ADT to PBRT to prevent progression in prostate cancer. To our knowledge, these are the first such findings to show that extending salvage radiotherapy to treat the pelvic lymph nodes when combined with short-term ADT results in meaningful reductions in progression after prostatectomy in patients with prostate cancer.

On the Lighter Side

"Are you enjoying your complimentary private accomodations?"

"And in recognition of your 20 years' loyal service in the X-ray department ..."

"Take one of these with water half an hour before you wake up every morning."

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet is available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org or Bill 619-370-8789 to coordinate.

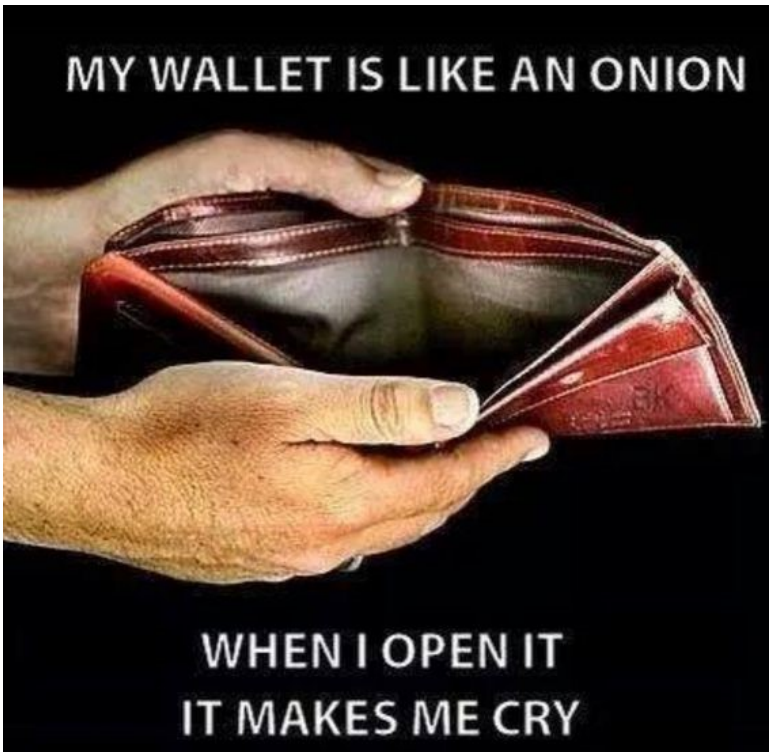
Member John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: https://ipcsg.org/personal-experience

Our brochure provides the group philosophy and explains our goals. Copies may be obtained by mail or email on request. Please pass them along to friends and contacts.

FINANCES

We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!



While our monthly meetings are suspended, we still have continuing needs, but no monthly collection. If you have the internet you can contribute easily by going to our website, http://ipcsg.org and clicking on "Donate" Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 420142, San Diego CA 92142

Editors Notes, Continued from Page 2

6. AUA 2022: Implementation of Germline Testing in Prostate Cancer *One of the limitations to the adoption of genetic testing in prostate cancer has been an inability to identify common, high prevalence alterations*
7. Embracing the Practical Aspects of Theranostics With Prostate-Specific Membrane Antigen–Targeted Lutetium-177 *What can you expect in radiopharma therapy*
8. Real-world use of MRI for risk stratification prior to prostate biopsy - *MRI can eliminate a lot of AS biopsies.*
9. Prostate diseases and microbiome in the prostate, gut, and urine– *bacteria have role in PCa development*
10. Association between baseline body mass index and survival in men with metastatic hormone-sensitive prostate cancer: ECOG-ACRIN CHAARTED E3805 *BMI doesn't affect mortality?*
11. Novel risk score for the risk of prostate cancer mortality | RRU *P-score gives better mortality est.*
12. New Guideline Gives Active Surveillance a Boost *AUA & ASTRO boost AS for low risk group*
13. Apalutamide plus Zytiga and prednisone Delays Progression of Metastatic Castration-Resistant Prostate Cancer. — *the men in the triple treatment group lived 24 months (median) without signs of disease progression, compared to 16.6 months for those in the standard of care control group*
14. Obesity associated with a higher risk of fatal prostate cancer, biggest study of its kind finds - *Every five-point increase in BMI was found to increase the risk of dying from prostate cancer by 10 per cent, while a 5 per cent increase in total body fat percentage raised the risk by 3 per cent.*
15. Targeted Radioligand Approved for Metastatic Prostate Cancer- *A therapy that uses a ligand to deliver a therapeutic radioisotope to individual cancer cells throughout the body gained FDA approval for certain patients with metastatic prostate cancer.*
16. Current and projected number of years of life lost due to prostate cancer: A global study- *In 2020, 3.5 million person-years of life were lost due to prostate cancer in males over 50, and 40% of YLL were in those aged over 75*

Benefits of PSA prostate cancer screening found to be more favorable than previous estimates, especially for blacks

eurekalert.org

New research led by investigators from Weill Cornell Medicine, Fred Hutchinson Cancer Center, University Hospitals Cleveland and Case Western Reserve University found that prostate cancer screening with the prostate specific antigen (PSA) blood test has remarkably favorable tradeoffs. This is particularly true for Black men, the investigators found, who disproportionately bear the burden of prostate cancer mortality and morbidity, and who are underrepresented in clinical trials.

Using epidemiologic data spanning a greater time period than previous estimates, the investigators produced new calculations of the number of men who were diagnosed and treated as a consequence of PSA screening as compared to the number of cancer deaths avoided. Their findings were published May 15 in *NEJM Evidence.*

Previous calculations over a decade ago estimated that, at best, one death was prevented for every 23 men diagnosed with prostate cancer as a consequence of screening. This suggested that too many men were experiencing the negative effects of a prostate cancer diagnosis as compared to those who benefit to recommend use of the screening test.

For their calculations, lead author Dr. Spyridon Basourakos, a resident in urology at Weill Cornell Medicine and NewYork-Presbyterian/Weill Cornell Medical Center, and colleagues improved on the previous estimates of overdiagnoses and overtreatment. Namely,

Articles of Interest continued from page 9

they included 11 more years of data than prior estimates; calculated estimates for men of all races and Black men; and used complementary approaches to estimating overdiagnosis.

Under conservative assumptions about screening's benefits, the investigators estimated that for men of all races one death was prevented for every 11 to 14 men diagnosed with prostate cancer and every 7 to 11 men treated for the disease. For Black men screening resulted in one death prevented for every 8 to 12 men diagnosed, and every 5 to 9 men treated. For more optimistic assumptions about screening, these tradeoffs were even more favorable, with numbers needed to treat in the low single digits for Black men.

The new analysis supports PSA screening, particularly for Black men and others at high risk, and highlight the need to revise clinical guidelines to accurately reflect the value of screening, the authors wrote.

Lead author: Dr. Spyridon Basourakos, Weill Cornell Medicine
Corresponding author: Dr. Jonathan Shoag, Case Western Reserve University, Weill Cornell Medicine

AUA 2022: Implementation of Germline Testing in Prostate Cancer

urotoday.com

(UroToday.com) In a podium presentation at the 2022 Society of Urologic Oncology Meeting held in conjunction with the American Urologic Association Annual Meeting held in New Orleans and virtually, Dr. Giri discussed the implementation of germline testing.

She first addressed the question of the role of germline testing in prostate cancer and clinical implications. In doing so, she began with a discussion of the historical context. Genetic testing for breast and ovarian cancer began in routine clinical practice more than two decades ago. BRCA testing (and other focused gene testing) became standard of care with risk assessment. Shortly thereafter, Lynch Syndrome testing also gained rapid uptake. However, in prostate cancer, this has taken much longer. Testing has also manifested somewhat differently with multigene testing used to inform precision medicine approaches.

One of the limitations to the adoption of genetic testing in prostate cancer has been an inability to identify common, high prevalence alterations. While pathogenic mutations are seen in 5-7% of patients with early stage disease and 10-15% of those with metastatic disease, a large number of different mutations account for this and the most common of these (eg. BRCA) are found in no more than 4% of patients.

In part for this reason and partly due to the changing landscape of genetic testing, she emphasized that there has been a migration from criteria driven genetic testing to criteria free testing. In the current, criteria free, model, affected patients with relevant tumor types may undergo genetic testing to drive precision therapy, clinical trial eligibility, cancer screening for additional tumor types, and cascade testing.

Among the many identified pathogenic mutations in prostate cancer, Dr. Giri emphasized that there are differential implications. Some of these may provide prognostic information while not being actionable, such as HOXB13. However, others including BRCA1 and 2 may have direct, clinically actionable implications. In most cases, the clinical actionability of these relates to eligibility for novel targeted treatments including PARP inhibitors (in the base of homologous recombination repair deficiency) or immune checkpoint inhibitors (in the case of microsatellite instability). Additionally, they may have implications for clinical trial eligibility.

Dr. Giri, in this context, discussed the results of the PROfound trial, a phase III randomized controlled trial of the PARP inhibitor olaparib. This trial was designed with biomarker inclusion (requiring alterations in one of 15 genes involved in homologous recombination repair) and biomarker stratification (with cohort A defined as those with alterations in BRCA1, BRCA2, or ATM and cohort B comprising the remainder). This study showed a significant benefit to olaparib compared to novel hormonal agent switch and led to FDA approval for this treatment approach in this biomarker selected population.

However, alterations such as BRCA2 may have important implications for patients earlier in the disease trajectory: work from the Johns Hopkins group has shown that for patients otherwise well suited for active surveillance, progression is much more common among those men with BRCA alterations.

Further, it should be noted that for patients with these alterations, there may be important implications for their family members in a manner that dramatically changes their health care, even when there are not direct, clinically actionable implications for the proband, so called cascade testing. The IMPACT trial has demonstrated that BRCA2 carriers have a higher cancer incidence rate, are diagnosed at a younger age, and are more likely to have clinically significant disease than non-carriers. Thus, among patients with know BRCA2 alterations, the NCCN guidelines recommend starting prostate cancer screening at age 40.

Highlighting that prostate cancer germline testing guidance may come from many guidelines, she emphasized that this is appropriate for patients with metastatic disease, regional/nodal disease, intraductal/cribriform histology, with high and very-high risk localized disease, with Ashkenazi Jewish heritage, or with relevant family history.

Second, she considered the principles of genetic counseling and genetic testing. Traditionally, this has been driven by genetic counselors who provide pre-test counseling followed by a post-test discussion of results and implications. Increasingly, clinicians are taking on the role of pre-test counseling with referral to genetics counselors reserved for those patients with evidence of alterations on testing. Given this increasing burden on clinicians, she cited the recent Philadelphia consensus which provides an implementation framework for prostate cancer genetic evaluation and management.

Finally, she addressed questions relating to the implementation of genetics care delivery models, highlighting many ongoing efforts and opportunities within her research program. She first noted the helix webtool (helix.guide) which provides provider education and clinical use guidance regarding prostate cancer genetic testing. This tool asks a variety of intake questions regarding patient demographic and disease characteristics to help guide clinicians. It further has education modules to help clinicians develop comfort and familiarity in this area. She then discussed the ENGAGEMENT study which, through recordings of case conferences, allows access to a multi-disciplinary approach to prostate cancer genetics care and a virtual genetics board.

Lastly, she discussed the EMPOWeR study which assessed the role of self-directed pretest video-based genetic education, rather than meeting with a genetics counselor.

Dr. Giri, therefore, concluded that genetic testing has become central to the management of prostate cancer. Understanding when and why it is indicated is critical for all physicians treating prostate cancer. Close collaboration between genetics counselors, oncology, urology, and primary care is critical to manage this rapidly evolving space.

Presented by: Veda Giri, MD, Sidney Kimmel Cancer Center, Thomas Jefferson University

Written by: Christopher J.D. Wallis, University of Toronto Twitter: @WallisCJD during the 2022 American Urological Association (AUA) Annual Meeting, New Orleans, LA, Fri, May 13 – Mon, May 16, 2022.

Embracing the Practical Aspects of Theranostics With Prostate-Specific Membrane Antigen–Targeted Lutetium-177[excerpt]

sciencedirect.com

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Outline

Abstract

Treatment options for men with metastatic castration-resistant prostate cancer are rapidly changing. In addition to novel anti-androgens and taxane-based chemotherapy, radiopharmaceuticals are having an increasing role. Although calcium-mimetic theranostics have been in use for years, newer approaches use molecularly targeted radiation therapy by conjugating isotopes to prostate-specific membrane antigen (PSMA) and in so doing directly target prostate cancer cells; ^{177}Lutetium-PSMA-617 is perhaps the best-known member of this new class. Expanding our capacity to deliver targeted beta-emitters requires additional planning and equipment. Having delivered close to 200 doses of ^{177}Lutetium-PSMA-617 at our center, we offer practical advice about patient selection, radiation safety, treatment administration, and toxicity monitoring. Although this blueprint is not the only way to expand a theranostics program beyond Radium-223, we offer our institutional experience with ^{177}Lutetium-PSMA-617 as an example to programs seeking to expand their radiopharmaceutical programs. We must rise to meet the patient-driven demand for these innovative and effective therapies.

Introduction

Options available to men with metastatic castration-resistant prostate cancer (mCRPC) have evolved rapidly, particularly in the second- and third-line setting. In particular, molecularly targeted radiopharmaceuticals, agents comprised of radioactive isotopes conjugated to targeting molecules for diagnostic or treatment purposes, have an increasingly important role.

The landmark ALSYMPCA trial established the alpha-emitter Radium-223 as an effective therapeutic option for men with mCRPC, finding Radium-223 improved overall survival and reduced skeletal-related events.[1] Its activity is attributed to its calcium mimetic properties, which allow localization to bone. By contrast, prostate-specific membrane antigen (PSMA)–conjugated theranostics target prostate cancer cells directly, using the PSMA transmembrane protein, which is overexpressed in prostate cancer.[2] Although a number of molecularly targeted radioisotopes are in development, the beta-particle emitter ^{177}Lutetium (^{177}Lu) is the best-known PSMA-targeted therapy. Its efficacy has been established by 2 recent randomized trials: TheraP[3] and VISION.[4]

As ^{177}Lu-PSMA-617 moves from the experimental realm into routine clinical practice, both radiation oncology and nuclear radiology programs will need guidance as they seek to add this therapeutic option to their armamentarium. We have given nearly 200 doses of ^{177}Lu-PSMA-617 in a safe and efficient manner. We will share what our center has learned.

Empty Cell	Position	Comments
1.	Physician AU	Can be either a radiation oncologist or a nuclear medicine physician
2.	Medical oncologist	At our center, medical oncologists do the initial patient eligibility screening, referral to the physician AU, and help to monitor toxic effects and PSA response
3.	Medical physicist AU	Physicist AU performs quality assurance, hot laboratory maintenance, calibration and dose verification, and maintenance of records, and ensures regulatory standard adherence
4.	Nurse	Nurses place intravenous drip feeds (IVs), obtain vital signs, and monitor patients post-injection
5.	Research team	^{177}Lutetium-PSMA-617 is not yet approved by the United States Food and Drug Administration; thus, responsibilities include interface with institutional review board, ordering and scheduling of doses, and reporting physician-identified adverse events
6.	Radiation safety officer	Responsible for leading the local radiation safety committee, maintaining the radioactive materials license, and ensuring that any generated radioactive waste is appropriately handled and has a place to decay appropriately

Abbreviations: AU = authorized user; PSMA = prostate-specific membrane antigen; PSA = prostate specific antigen.

Abbreviation: PSMA = prostate-specific membrane antigen.

Patient Selection and Intake

Appropriate patient selection is key to optimizing patient outcomes. For patients accessing ^{177}Lu-PSMA-617 through the managed access program, all had to meet the criteria defined by the VISION trial. These patient eligibility criteria are found in Table 3.

Table 3. ^{177}Lutetium-PSMA-617 patient eligibility criteria

	VISION patient eligibility criteria
1.	Adult men with metastatic castration-resistant prostate cancer and: at least 1 PSMA-positive metastatic lesion on PSMA positron emission tomography/computed tomography •no PSMA-positive visceral lesions >1 cm; no PSMA-negative lesions
2.	A documented progression on at least: •1 line of taxane-based chemotherapy and novel antiandrogen therapies
3.	A life expectancy >6 mo
4.	Adequate laboratory values •Platelets >100 k/μL, hemoglobin >9 g/dL, neutrophil count >1.5 k/μL, adequate kidney and liver function (CBC w/diff, CMP)

Abbreviations: CBC w/diff, CMP = complete blood count with differential, complete metabolic count; PSMA = prostate-specific membrane antigen.

For ease of multidisciplinary coordination, our practice for these patients is as follows:

1.Patients present to medical oncology, where treatment options/alternatives, performance status, conventional imaging, treatment history, and laboratory parameters are reviewed.

2.If ^{177}Lu-PSMA-617 is being considered, medical oncology will assess whether the patient has had PSMA positron emission tomography/computed tomography (CT) and arrange for an on-site visit, if needed, to obtain this scan.

3.Patients are seen back by the medical oncology team to review all results. Those patients who meet eligibility criteria (Table 3) and for whom ^{177}Lu-PSMA-617 is believed to be the best therapeutic option are then referred to radiation oncology.

4Our radiation oncology physician authorized user (AU) meets with the patient, provides information and counseling related to the treatment and posttreatment recommendations, and performs an independent evaluation of the patient's suitability for ^{177}Lu-PSMA-617. Urinary continence assessment is important.

5.Once the physician AU approves the patient for treatment, medical oncology and our research team take steps to request the dose of ^{177}Lu-PSMA-617.

6.Once the ^{177}Lu-PSMA-617 delivery date is secured, the physician AU places the patient on the radiation oncology schedule for 4 to 6 scheduled administrations of 7.4 GBq (200 milicuries; note that the half-life of ^{177}Lu is 6.7 days) at 6-week intervals.

Abbreviations: ^{177}Lu = ^{177}Lutetium; ALARA = as low as reasonably achievable; AU = authorized user; MD AU = physician authorized user; CT = computed tomography; IV = intravenous/intravenous drip feed; PSMA = prostate-specific membrane antigen.

We order patient-specific doses of ^{177}Lu-PSMA-617 via the website of the company, which ships the drug 14 days in advance of dosing. We receive each patient dose at our department by currier, and our team completes required Department of Transportation paperwork upon receipt. Our AU physicists remove the lead "pig" from the shipping box and do initial quality assurance in our department hot laboratory, in a space lined with lead blocks, behind a device with lead glass and adorned with all needed radiation safety equipment described in Table 2. At our center, the AU physician draws up the dose into a labeled syringe, which is then put in a beta-emitter shield, and placed inside a lead igloo, for transport to our CT room.

Conclusion

The favorable treatment responses and survival benefit reported in the TheraP and VISION trials resulted in ^{177}Lu-PSMA-617 receiving FDA breakthrough therapy designation for men with mCRPC. As a result, the number of patients seeking to access this therapy has increased at our clinic. Meeting this patient demand requires that radiation oncology and nuclear medicine centers expand their theranostics programs. We hope this practical guide will help other centers seeking to develop the capacity to deliver this innovative therapy.

Real-world use of MRI for risk stratification prior to prostate biopsy

nature.com
Ross, Ashley E.

Abstract

Background

The utilization of MRI to risk stratify elevated PSA prior to prostate biopsy has been inconsistently adopted and varies considerably by practice setting. This study aims to evaluate the usage and performance of MRI as an advanced risk stratification tool of elevated PSA prior to biopsy and identify factors associated with differential utilization of MRI at a large academic setting with ready access to 3T multiparametric MRI of the prostate.

Methods

A retrospective single-center study of 2900 men presenting with elevated PSA 2–20 ng/mL from 2018 through 2021 was conducted. We analyzed trends in MRI utilization and outcomes of prostate biopsy by MRI usage. Univariate and multivariate logistic regressions were performed to calculate odds ratios to identify patient- and provider-level predictors of MRI usage.

Results

Rates of prebiopsy MRI utilization increased from 56% in 2018 to 89% in 2021 ($p < 0.001$). Prebiopsy MRI led to biopsy avoidance in 31% of men. MRI usage enhanced detection of clinically significant prostate cancer by 13% and reduced identification of Gleason Grade Group 1 disease by 3% and negative biopsies by 10% ($p < 0.001$). Men who received MRI were more likely to be younger than 75 years in age and have private or Medicare insurance, PSA >4 ng/mL, and PHI >27. In both univariate and multivariate analysis, black race and Medicaid insurance were associated with reduced MRI utilization (all $p < 0.001$). Urologic provider was an independent predictor of MRI usage ($p < 0.001$).

Conclusions

Use of MRI as a risk stratification tool for elevated PSA rose during this 4-year study period. Men who self-identify as black or men with Medicaid coverage have diminished rates of MRI usage. Considerable provider-level variability in MRI use was observed. Future research aimed at identifying factors affecting implementation of MRI as a routine risk assessment tool is warranted.

Contributions

MRS led the study from conception to completion and prepared the manuscript. BA, PVS, JAA, and EVL assisted in data clean-up and manuscript preparation. JMR and AKM helped with data clean-up as well. SASM, M-KK, and QM helped with data processing. XM provided biostats assistance. EMS and AER are senior authors who guided all of the aforementioned processes from study conception to its completion.

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Prostate diseases and microbiome in the prostate, gut, and urine

docwirenews.com

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ABSTRACT

The microbiome in various organs involves a vast network that plays a key role in the health and wellness of the human body. With recent advances in biological technologies such as high-throughput sequencing, transcriptomics, and metabolomics, it appears that the microbial signature varies dynamically among individuals, creating various roles in metabolism, local and systemic inflammation, and host immunity. Urinary and genital organs, including the prostate, seminal vesicles, and urinary bladder, are reservoirs of several bacterial, viral, and fungal communities. Accumulating evidence has suggested profound roles for the gut, urinary, and intraprostate microbiomes in genitourinary benign and malignant diseases. This review article addresses microbiome-related evidence for three major diseases involved in prostate cancer: chronic prostatitis (CP), benign prostatic hyperplasia (BPH), and prostate cancer (PCa). Symptomatic CP is known as CP/chronic pelvic pain syndrome. CP is one of the most common prostate diseases in young men, accounting for 8% of all men visiting a urologic clinic. Although oral medication is the gold standard therapy for patients with BPH, approximately 13% of men present with clinical progression within 4 years after the initiation of treatment, with 5% requiring surgical intervention. The identification of proinflammatory cytokines and pathogens responsible for the clinical progression of BPH is still underway. Several topics regarding the association between PCa and the microbiome are discussed in this review as follows: i) intraprostatic microbiome and the risk of PCa, ii) gut microbiome and PCa, iii) gut microbiome and the risk of radiation-induced side effects, iv) isoflavone intake and equol-producing intestinal flora on PCa, and v) the inhibitory effect of daidzein and equol on tumor growth and progression of PCa. Further studies are required for a comprehensive understanding between the urogenital microbiome and prostate pathogenesis to facilitate the development of preventive and therapeutic approaches for prostate diseases.

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Association between baseline body mass index and survival in men with metastatic hormone-sensitive prostate cancer: ECOG-ACRIN CHAARTED E3805

onlinelibrary.wiley.com

Alicia K. Morgans MD

Abstract

Background

E3805 (CHAARTED) is a phase 3 trial demonstrating improved survival for men with metastatic hormone-sensitive prostate cancer (mHSPC) randomized to treatment with docetaxel (D) and androgen-deprivation therapy (ADT) versus ADT alone. We assessed the association of baseline body mass index (BMI) and metformin exposure with quality of life (QOL) and prostate cancer outcomes including survival in patients enrolled in the CHAARTED study.

Methods

We performed a posthoc exploratory analysis of the CHAARTED trial of men with mHSPC randomized to treatment with ADT with or without D between 2006 and 2012. Cox proportional hazards models and Kruskal–Wallis test were used to evaluate the association between BMI with QOL and prostate cancer outcomes and between metformin exposure and survival.

Results

In 788 of 790 enrolled patients with prospectively recorded baseline BMI and metformin exposure status, lower BMI was not associated with survival, but was associated with high volume disease ($p < 0.0001$) and poorer baseline QOL on functional assessment of cancer therapy–prostate ($p = 0.008$). Only 68 patients had prevalent metformin exposure at baseline in the CHAARTED trial. Four groups were identified: ADT + D + metformin ($n = 39$); ADT + D ($n = 357$); ADT + metformin ($n = 29$); and ADT alone ($n = 363$). Baseline clinicopathologic characteristics were similar between groups. In this small exploratory multivariable analysis, metformin exposure was not associated with survival (hazard ratio: 1.15; 95% confidence interval: 0.81–1.63, $p = 0.44$).

Conclusions

There was no link between baseline BMI and survival, but lower baseline BMI was associated with features of greater cancer burden and poorer QOL.

Novel risk score for the risk of prostate cancer mortality | RRU

dovepress.com
Dove Press

Introduction

Prostate cancer (PCa) is one of the most common types of cancer in men; over 470,000 men were diagnosed with the disease in Europe during 2020.[1] Since the emergence of prostate-specific antigen (PSA) testing in the early 1990s, incidence rates have risen considerably in Western countries.[2] Standard treatment of PCa includes radical prostatectomy, radiation and hormone therapy, as well as conservative approaches, such as active surveillance.[3,4]

Prostate cancer is a highly heterogeneous disease and while some tumors are aggressive and require invasive treatment, most prostatic malignancies are indolent and unlikely to progress to clinically significant PCa.[5,6] Despite a lifetime risk of being diagnosed with the disease of approximately 17%, the substantially lower 3% risk of dying from PCa indicates that many patients can be managed conservatively.[7] Nevertheless, a large proportion of PCa patients undergo radical treatment, suggesting that a considerable number of patients are over-treated.[5,6] Overtreatment is a concern because radical treatment frequently affects the patient's quality of life and leads to considerable healthcare expenses,[5,8] while not necessarily improving PCa-related survival outcomes compared to active surveillance.[6,7]

Currently, treatment decisions are mainly guided by clinicopathological parameters. The D'Amico classification system, a nomogram based on PSA, clinical tumor stage (T-stage), and Gleason Score (GS), is widely used to stratify PCa patients into low-, intermediate- and high-risk groups.[9] There is, however, evidence of marked heterogeneity in outcomes among patients assigned to the intermediate-risk group based on the D'Amico classification system. This suggests that a subset of patients in this intermediate risk category harbor indolent tumors, causing uncertainty about the necessity of radical interventions.[10] Similarly, heterogeneous outcomes among patients assigned to the intermediate risk group according to the National Comprehensive Cancer Network (NCCN) guidelines have been reported,[11] although this has been improved by subdividing patients into favorable and unfavorable intermediate risk groups.[4,12] Nevertheless, more reliable risk stratification systems are needed to guide decision-making and to avoid overtreatment of patients with clinically insignificant lesions while ensuring adequate therapeutic intervention for those with aggressive tumors.

Recently, genetic biomarkers have been identified and incorporated into risk scoring systems, providing improved prognostic value compared to traditional nomograms, which are based on clinical and pathological parameters only.[13] However, introduction into clinical practice is slow, and data on their impact on clinical decision-making and patient outcomes is limited.[4]

In a previous study, Peng et al identified a three-gene signature which correlated with PCa-specific survival, independent of clinical parameters.[14] The authors first identified 641 embryonic stem cell (ESC) gene predictors (ESCGPs) using publicly available datasets of whole-genome cDNA microarrays from five human ESC lines and 115 human normal tissues. Using prostate fine-needle aspiration samples from a Swedish cohort of 189 PCa patients diagnosed between 1986 and 2001, the authors found that three of these genes, insulin-like growth factor-binding protein 3 (IGFBP3), coagulation factor III (thromboplastin, tissue factor, F3), and vestigial-like family member 3 (VGLL3) correlated with PCa-specific survival. In this cohort, the three-gene signature showed improved predictive value for estimating the risk of PCa-specific mortality at diagnosis, independent of age, PSA level, tumor grade and clinical stage.[14]

The present retrospective study is a continuation of the work led by Dr. Peng and summarizes the development and validation of a novel risk score, the Prostatype risk score (P-score), based on this three-gene signature and clinicopathological parameters, in a larger, modern cohort with up to eleven years of survival data. The P-score is intended to guide treatment decisions for patients with newly diagnosed PCa.

- - -

Conclusion

In conclusion, we developed the P-score, a risk stratification system for newly diagnosed PCa patients by integrating an ESC gene-signature measured in FFPE tumor tissue from PCa patients. The P-score was validated and showed superior performance in predicting PCa-specific mortality, compared to existing standard risk classification systems. Our findings support the clinical utility of the P-score for accurately distinguishing between patients likely to experience favorable or unfavorable outcomes. Consequently, it would be expected that using the P-score will reduce overtreatment of PCa patients, while ensuring that individuals with high-risk disease are treated appropriately. Therefore, the P-score could provide urologists with a valuable decision support tool to identify PCa patients most likely to benefit from curative treatment while simultaneously reducing overtreatment.

New Guideline Gives Active Surveillance a Boost

medscape.com

Howard Wolinsky

Two major medical groups strengthened their recommendations for active surveillance (AS) for patients with low-risk prostate cancer and for the first time recommended the approach for some patients with favorable intermediate-risk prostate cancer.

Experts hailed the new guidelines, released May 10 by the American Urological Association (AUA) and the American Society for Radiation Oncology (ASTRO), as a boon for patients with low-risk to favorable intermediate-risk prostate cancers.

Dr James Eastham

"The guideline is unequivocal that AS is the preferred management option for the majority of men with low-risk prostate cancer," panel chair James A. Eastham, MD, Peter T. Scardino Chair in Oncology and chief of urology at Memorial Sloan Kettering Cancer Center, New York City, told *Medscape Medical News*.

The new guideline is the first guideline for localized prostate cancer since 2017.

In the new document, guideline writers merged low-risk patients and very-low-risk patients into a single category of "low-risk." Eastham said a distinction between very-low-risk and low-risk is inconsequential since the treatment for the two groups of patients is identical.

The 2022 guideline for the first time makes AS the recommended treatment for select patients with favorable

intermediate-risk Gleason 3+4 prostate cancer, he said. The document also provides guidance on how such patients should be selected for AS.

Most research suggests that as many as 40% of patients newly diagnosed with prostate cancer have low-risk disease. Favorable intermediate-risk cancer represents 10% to 15% of newly diagnosed patients, said Todd Morgan, MD, the Jack Lapides, MD, Research Professor and chief of urologic oncology at Michigan Medicine, Ann Arbor.

Morgan, who was not on the AUA/ASTRO panel, called the new recommendations "a very strong update compared to the guideline from 5 years ago."

The guideline has been pared back some from 2017 to include fewer statements, but it covers several key clinical trials that have appeared over the past 6 years to strengthen the evidence base for the document, he said.

"I would say that we still have to acknowledge that many statements are based on 'expert opinion' rather than high-level evidence, which highlights the continued need for well-conducted studies that prove or disprove some of these statements," Morgan added.

Patients Weighed In

This year, AUA's advocacy group urged patients to comment on the proposed guideline.

Rick Davis

Rick Davis, founder of the AnCan Foundation, a virtual support network for prostate cancer and other diseases, thanked the groups for acknowledging the value of peer support and virtual support groups.

cancerabcs.org

Apalutamide plus Zytiga and prednisone Delays Progression of Metastatic Castration-Resistant Prostate Cancer. — Cancer ABCs

Findings of a phase 3 clinical trial indicate that the combination of Zytiga (abiraterone), prednisone and Erleada (apalutamide) can delay the progression of metastatic castrate-resistant prostate cancer. The findings were published in *The Lancet Oncology* on September 30, 2021, by an international research team led by Dr. Fred Saad, a researcher at the CHUM Research Centre, a Université de Montréal professor and the holder of the Raymond Garneau Chair in Prostate Cancer Research.

The trial was a collaboration with 167 hospitals in 17 countries. The study, called ACIS, identified for the first time a combination of three drugs that slowed the progression of metastases by more than seven months. This finding is a significant therapeutic breakthrough for treating advanced prostate cancer.

The trial evaluated 982 men between the end of 2014 and the middle of 2016 and divided them randomly into two groups (randomized, double-blind trial). Of the volunteers, 492 received apalutamide (an anti-androgen) combined with abiraterone (an androgen synthesis inhibitor) and prednisone (an anti-inflammatory drug).

The control group of 490 men received only abiraterone and prednisone. This well-tolerated therapeutic trio was administered to men with metastatic castration-resistant prostate cancer. Prostate cancer is considered castration-resistant when cancer progresses despite hormone therapy.

By following the progression of the cancer through radiologic scans, the researchers were able to show that the men in the triple treatment group lived 24 months (median) without signs of disease progression, compared to 16.6 months for those in the standard of care control group.

The researchers have suggested that additional studies will help to accurately identify the sub-categories of men who would most benefit from this combination of drugs.

At Cancer ABCs, we acknowledge the great value that the many current, ongoing clinical trials of combinations of approved drugs can bring to our treatment protocol. However, we suggest that, in addition to combination studies, there need to be other studies that evaluate the survival benefit of sequencing the same drugs and comparing these results to the combination trials. Included in the comparison, we wish to see an evaluation of patient-reported side effects between the sequenced and combination trials.

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The article "Apalutamide plus abiraterone acetate and prednisone versus placebo plus abiraterone and prednisone in metastatic, castration-resistant prostate cancer (ACIS): a randomized, placebo-controlled, double-blind, multinational, phase 3 study" by Dr. Fred Saad and his colleagues was published on September 30, 2021, in The Lancet Oncology.

Obesity associated with a higher risk of fatal prostate cancer, biggest study of its kind finds - EASO

easo.org

Every 10cm (four inches) on waist increases risk of fatal disease by 7 per cent, data from 2.5 million men reveals.

1,300 prostate cancer deaths a year in the UK might be avoided if average BMI in men was five points lower.

A new study presented at this year's congress in Maastricht (poster PO2.33) and published simultaneously in the journal *BMC Medicine,* has linked body fat (adiposity) with risk of fatal prostate cancer.

It found that every 10cm (3.9 inches) on a man's waist increased his odds of dying from prostate cancer by 7 per cent. The association didn't just apply to belly fat, however, with the rise in risk similar for overall body fatness.

Prostate cancer is the most common cancer in men in the UK, with around 52,000 cases a year. It is also the second most common cause of cancer death in males in the UK, with almost 12,000 deaths annually.

"Knowing more about factors that increase the risk of prostate cancer is key to preventing it," says Dr Aurora Perez-Cornago, of the Cancer Epidemiology Unit, Oxford Population Health, University of Oxford, UK, who led the research.

"Age, family history and black ethnicity are known risk factors but they are not modifiable, and so it is important to discover risk factors that it is possible to change."

In addition, although many prostate cancers are slow-growing and may not cause a man harm during his lifetime, others are lethal and these may have different risk factors.

Some previous studies have suggested that higher adiposity (amount of body fat) is a risk factor for lethal prostate cancer, with central adiposity (fat around the belly and waist) being particularly important.

However, the small number of prostate cancer deaths included in individual studies have made it hard to draw firm conclusions.

To find out more, Dr Perez-Cornago and colleagues put data from multiple published studies together in a meta-analysis.

Funded by Cancer Research UK, it was the biggest meta-analysis of its kind. It included data on 2.5 million men from 19 studies on the PubMed, Embase and Web of Science databases, as well as data from a new analysis of data from more than 200,000 men in the UK Biobank study.

All of the studies included in the meta-analysis were prospective, meaning men who were free of prostate cancer at the start of the study were followed for many years and the number of deaths from prostate cancer during that time logged.

Adiposity was measured at the start of each study, with up to four different measures used: body mass index (BMI, a measure of body fat based on weight and height, available for 19,633 men who subsequently died from prostate cancer), waist circumference (3,181 deaths), waist to hip ratio (1,639 deaths) and body fat percentage (670 deaths).

Higher amounts of body fat (adiposity) were linked to higher likelihood of fatal prostate cancer.

Every five-point increase in BMI was found to increase the risk of dying from prostate cancer by 10 per cent, while a 5 per cent increase in total body fat percentage raised the risk by 3 per cent.

The risk was similarly increased for central adiposity. Each 0.05 increase in waist to hip ratio increased the risk of fatal prostate cancer by 6 per cent. And every 10 cm (3.9 inch) increase in waist circumference increased the odds by 7 per cent.

The researchers also calculated that there would be around 1,300 fewer prostate cancer deaths a year in the UK if the average BMI in men was five points lower.

The study's authors conclude: "We found that men with higher total and central adiposity have a higher risk of dying from prostate cancer than men with a healthy weight."

It isn't clear what is behind the link, says Dr Perez-Cornago. Several biological mechanisms have been proposed. It is likely, however, that differences in detection also play a role. The disease may be harder to detect in

men with obesity, leading to it being diagnosed later when it is harder to treat.

Dr Perez-Cornago adds: "More research is needed to determine if the association is biologically driven or due to delays in detection in men with higher adiposity. In either case, our latest results provide another reason for men to try to maintain a healthy weight."

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Article available here (to be deactivated after congress)

Targeted Radioligand Approved for Metastatic Prostate Cancer

Howard D. Larkin

jamanetwork.com

A therapy that uses a ligand to deliver a therapeutic radioisotope to individual cancer cells throughout the body gained FDA approval for certain patients with metastatic prostate cancer. When the ligand binds with a cancer cell, the attached radiotherapeutic agent kills or interferes with the cell's reproduction, as well as that of nearby cells.

Lutetium Lu 177 vipivotide tetraxetan (formerly called ^{177}Lu-PSMA-617), marketed as Pluvicto, is an add-on injection therapy for patients with prostate–specific membrane antigen (PSMA)–positive metastatic castration–resistant prostate cancer (mCRPC) who have previously been treated with androgen receptor pathway inhibition and taxane-based chemotherapy. Studies are underway to include patients earlier in treatment, according to a statement by manufacturer Advanced Accelerator Applications USA, Inc, a Novartis company.

The therapy is delivered by injection every 6 weeks for up to 6 doses. In a phase 3 study involving 831 patients, those receiving standard of care plus lutetium Lu 177 vipivotide tetraxetan had a significant reduction in risk of death with a median overall survival of 15.3 months compared with 11.3 months for the standard of care–only control group.

In a subgroup of 581 patients, imaging-based progression-free survival also was prolonged in the treatment group for a median 8.7 months compared with 3.4 months for the control group. These patients were randomized after a protocol change reduced dropouts in the control group, primarily from dissatisfaction, from 56% to 16.3%. Severe adverse events were more frequent in the treatment group, with grade 3 or higher events occurring in 52.7% of this group compared with 38% of the control group. However, quality of life mostly was not adversely affected as measured by a standardized assessment questionnaire.

The FDA also approved the first radioactive diagnostic agent for patient selection in the use of a radioligand therapeutic agent. Gallium Ga 68 gozetotide, marketed as Locametz, is a radioactive diagnostic agent for positron emission tomography of PSMA-positive lesions, including selecting patients for lutetium Lu 177 vipivotide tetraxetan therapy.

Current and projected number of years of life lost due to prostate cancer: A global study

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Diana Withrow PhD

Abstract

Background

Prostate cancer is an important cause of death worldwide. The number of years of life lost (YLL) due to pros-

tate cancer is a metric of the toll of prostate cancer and using projections of demographic changes, can be used to measure future burden.

Methods

Prostate cancer mortality data by country and world region was retrieved from the Global Cancer Observatory and the World Health Organization mortality data set, and life expectancy was from the United Nations Department of Economic and Social Affairs. We estimated YLL as the difference between age at death in people with prostate cancer and remaining life expectancy for people of the same age in the general population. We also estimated the age-standardized YLL rates per 100,000 males over 50 and the average annual percentage change in YLL rates over the period 2000–2019 and the number of YLL for the year 2040 by applying population projections to the 2020 YLL rates.

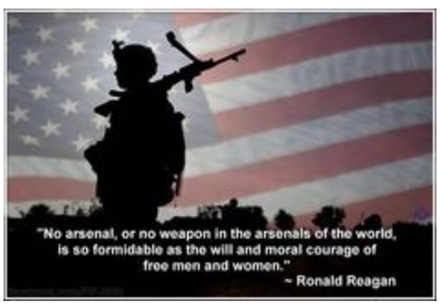
Results

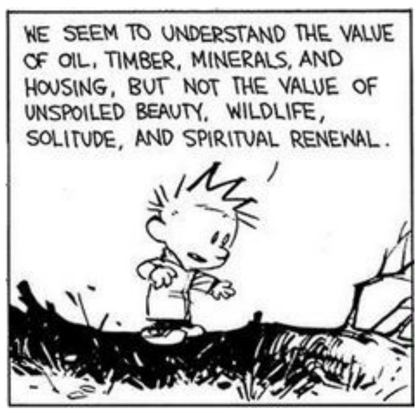
In 2020, 3.5 million person-years of life were lost due to prostate cancer in males over 50, and 40% of YLL were in those aged over 75. Age-standardized rates varied greatly between and within regions. Over the last two decades, rates of YLL have increased in many Asian and African countries while they have decreased in northern American and European countries. Globally, YLL are anticipated to double by 2040 to reach 7.5 million, with the greatest increases in Africa, Asia, and Latin America and the Caribbean.

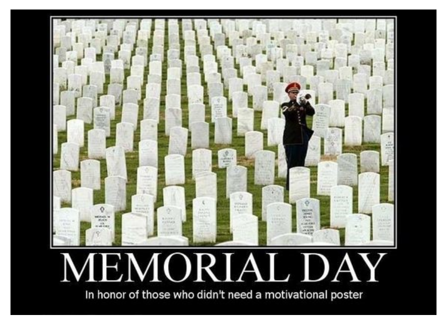
Conclusion

There are wide variations in the burden of prostate cancer globally as measured by YLL. The burden of prostate cancer is projected to increase over time and appears to be highest in Sub-Saharan Africa, Eastern Europe, and Latin America and the Caribbean. It will be critical to plan and implement programs to reduce the burden of prostate cancer globally.

On the Lighter Side







On the Lighter Side

"THAT'S HOW LEROY EXERCISES . . . HE CALLS IT A CONTROLLED BURN."

"It's a flashlight. I couldn't find any candles."