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

September 2020 NEWSLETTER

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Tuesday, September 15,

Volume 13 Issue 09

.Live-Stream Event, Saturday, September19th,10:00am PT

September 19 - Dr. Sumit Subudhi discusses the Immune System and PCa.

Dr Subudni is Assistant Professor, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston. He is a medical oncologist and immunologist whose research focuses on the mechanisms and pathways within the immune system that are responsible for tumor rejection and clinical benefit. Dr Subudhi Discussed Immune Checkpoint Inhibitors in Prostate Cancer at AJMC: In prostate cancer, he's using combinations by looking to see how one drug may trigger an immune infiltrate or proteins that allow the tumor to resist the monotherapy.

- **For further Reading: https://ipcsg.blogspot.com/**
- **For Comments, Ideas and Questions,** email to Newsletter@ipcsg.org

Social Security and Supplemental Plans

August 2020 Informed Prostate Cancer Support Group Online Presentation

Get to Know Medicare – Richard Russell

Summary by Bill Lewis

Top 10 Medicare Questions:

1. What is Medicare? It is a federal health insurance program for eligible U.S. citizens and legal residents, which is funded in part by taxes you pay while working. It is individual health insurance, not a family health plan, Social Security, Medicaid, or Free.

2. Who can get Medicare? U.S. citizens and legal residents (legal residents must live in the U.S. for at least 5 years in a row, including the 5 years just before applying for Medicare). You must also meet one of the following requirements: Age 65 or older; Younger than 65 with a qualifying disability; Any age with a diagnosis of end-stage renal disease or ALS.

3. What does Medicare cover? Original Medicare has two parts: Part A is hospital insurance, and covers hospital stays and inpatient care, including your hospital room and meals; Skilled nursing services; Care in special units, such as intensive care; Some blood transfusions; Drugs and medical supplies used during an inpatient stay; Hospice care, including medications to manage symptoms and pain; Lab tests, X-rays and medical equipment as an inpatient; Part-time, skilled care for the homebound after a qualified inpatient stay;
Operating room and recovery room services; Rehabilitation services after a qualified inpatient stay.

Additional facts about Part A: the premium is free forever, if you or your spouse worked and paid taxes for 10 years or longer. You can't be denied coverage. Coverage is nationwide, including any qualified hospital in the U.S. Coverage and costs are per "benefit period." You must be admitted as an inpatient (not on

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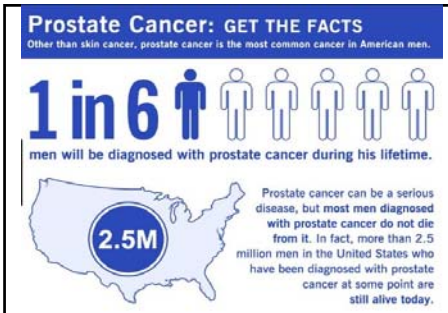

Organization

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

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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 through our website:
https://ipcsg.org/purchase-dvds

The DVD of each meeting will be available by the next meeting date.

From the Editor

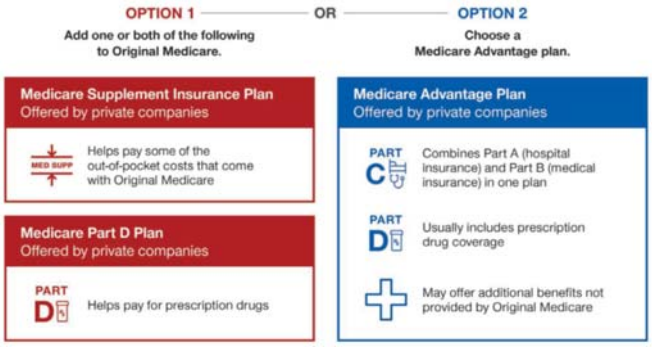
Due to COVID-19, no in-person meetings will be held until further notice. We will continue to post and distribute the newsletter in the interim. Our speaker this month will be streamed and broadcast via the group web site. In order to include more articles of interest in this issue, we have included extra pages in the web distributed version of the newsletter. The mail version is limited to ten pages.

Articles of Interest

- Novel insights of how prostate cancer causes secondary tumors
- 'Spare Tire' Increases Prostate Cancer Risk - MedicineNet Health News
- Delaying RT for Higher-Risk Prostate Cancer Found Safe
- Quantifying the Number of Cancer Deaths Avoided Due to Improvements in Cancer Survival since the 1980s in the Australian Population, 1985–2014
- Survival following upfront chemotherapy for treatment-naïve metastatic prostate cancer: a real-world retrospective cohort study
- Surgery Rates Doubled for High-Risk Prostate Cancer
- Protecting Your Bones and Improving Your Quality of Life During Prostate Cancer Treatment — Cancer ABCs
- Abiraterone and enzalutamide had different adverse effects on the cardiovascular system: a systematic review with pairwise and network meta-analyses
- Synergy between radiation of metastases and immunotherapy confirmed
- Prostate Theranostics - What the Hell? — Cancer ABCs

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** Lyle LaRosh @ 619-892-3888; or **Director** Gene Van Vleet @ 619-890-8447.



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"observation status"). It provides an additional 60 "lifetime reserve" days (see below).

Part B is medical insurance, and covers doctor visits and outpatient care, including doctor visits in the hospital; Diabetes screenings, education and certain supplies; An annual wellness visit and preventive services, like flu shots; Mental health care; Clinical laboratory services, like blood and urine tests; Durable medical equipment (DME) for use at home, like wheelchairs and walkers (if prescribed by doctor and obtained from a Medicare-approved vendor); X-rays, MRIs, CT scans, EKGs and some other diagnostic tests; Ambulatory surgery center services; Some health programs, like smoking cessation and obesity counseling; Ambulance and emergency room services; Physical therapy, occupational therapy and speech-language pathology services.

Additional information about Part B: It has a monthly premium (adjusted for what your income was 2 years earlier; $144.60 is typical in 2020). You can't be denied coverage. Coverage is nationwide, including any provider who accepts Medicare. There is a permanent/ongoing premium penalty for late enrollment.

"Original Medicare" (Parts A & B) does not cover all of the cost of your care – you have out-of-pocket costs, with no limit. It also does not cover Prescription drugs; Routine dental, vision or hearing care; Eyeglasses, contacts or hearing aids; Long-term or custodial care (help bathing, eating, dressing); Excess charges for services by doctors who don't accept Medicare assignment (where you have to pay the difference between what Medicare allows, and the doctor's actual fee, in addition to your percentage of what is allowed); or Care received outside the U.S., except for certain circumstances.

4. How much does Medicare cost? Your premium: A fixed amount that you pay for coverage, usually monthly. Plus, a Deductible: A set amount that you pay for covered services before your plan begins to pay anything. Also, a Copay: A fixed amount you pay at the time you receive a covered service. And Coinsurance: An amount you pay when the cost of a covered service is split with you by percentage, such as 80/20.

2020 Medicare Part A (Hospital) Costs: The premium is $0 for most people. The deductible: $1,408 per benefit period (up to 60 days) for being 1-60 days in the hospital. If released and later readmitted, there will be a new deductible to be paid. Other Costs: $352 per day for days 61–90 in one benefit period (one hospitalization); $704 per lifetime reserve day (maximum of 60 days beyond the above benefits). Note: there is NO out-of-pocket limit.

2020 Medicare Part B (Medical) Costs: The premium is $144.60 per month for most people. The deductible is $198 for the year. Other Costs: 20% of approved amount for most covered services. Excess charges (if any) – If you see doctors who don't accept the "assignment" (Medicare approved amount), you pay the additional amount to meet his fees, beyond the 20% you would always pay of the assignment amount. Note: As with Part A, there is NO out-of-pocket limit.

5. Where can I get more coverage?

Part C – "Medicare Advantage" – this is another way to get your Medicare benefits – An alternative to Original Medicare (Parts A & B). Plan members are still in the Medicare program (still have a contract with the government), but benefits are administered by the plan, which is offered by private insurance companies.

All Medicare Advantage plans cover: All the benefits of Part A (except hospice care, which is still covered by Part A) and all the benefits of Part B. Most Medicare Advantage plans also cover prescription drugs. Medicare Advantage plans may offer additional benefits and features, such as: Dental exams, cleanings and X-rays; Eye exams, eyeglasses and corrective lenses; Hearing tests and hearing aids; Wellness programs and fitness memberships. Note: Medicare Advantage plans have an annual out-of-pocket maximum to help protect the insured against high costs.

Types of Medicare Advantage plans: There are four "Coordinated-care" plans – Health Maintenance Organization plans (HMO; requires a referral from primary physician to see a specialist); Preferred Provider Organization plans (PPO – allows you to go outside the network, at extra cost); Point of Service plans (POS); and Special Needs Plans (SNP – for low income or chronic conditions; doctor's recommendation required). Two other plan types are Private Fee-For-Service plans (PFFS)

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Standardized Medicare Supplement Plans

Benefit	Plan A	Plan B	Plan C[1]	Plan D	Plan F[1]	Plan G	Plan K	Plan L	Plan M	Plan N
Part A hospital coinsurance and 365 extra hospital days	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Part A deductible		100%	100%	100%	100%	100%	50%	75%	50%	100%
Part B coinsurance or copays	100%	100%	100%	100%	100%	100%	50%	75%	100%	100%*
Part B annual deductible			100%		100%					
Part B excess charges					100%	100%				
Cost of blood transfusion (first 3 pints)	100%	100%	100%	100%	100%	100%	50%	75%	100%	100%
Cost of foreign travel emergency (up to the plan limits)			80%	80%	80%	80%			80%	80%
Hospice care coinsurance costs	100%	100%	100%	100%	100%	100%	50%	75%	100%	100%
Part B preventive care coinsurance	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Skilled nursing facility care coinsurance			100%	100%	100%	100%	50%	75%	100%	100%
Yearly out-of-pocket limit before all benefits paid at 100% (2020)							$5,880	$2,940		

*except certain copays

[1] Only available to beneficiaries who became eligible in 2019 or earlier, and who enrolled prior to January 1, 2020.

UnitedHealthcare

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and Medical Savings Account plans (MSA).

Additional facts about Medicare Advantage: You must be enrolled in both Medicare Part A and Part B and live in the plan service area; you can't be denied coverage based on current financial or health status, including pre-existing conditions (there are special rules for people with end-stage renal disease, starting in 2021); you may be required to use provider and pharmacy networks; coverage and costs vary by plan and may change each year; there is an annual limit on out-of-pocket costs for covered services; there may or not be a monthly plan premium charged; and you must continue to pay the Part B premium to Medicare.

Part D – Medicare Prescription Drug Coverage – Helps with the cost of prescription drugs. There are two ways to get coverage: Add a standalone Part D plan to Original Medicare, or choose a Medicare Advantage plan that includes prescription drug coverage. Part D plans are offered by private insurance companies. Part D plans cover the types of drugs most commonly prescribed for Medicare beneficiaries (as determined by federal standards). Specific brand name drugs as well as generic drugs are included in the drug list (formulary). Part D also covers commercially available vaccines not covered by Part B.

The formulary (the list of covered drugs) has the drugs grouped into 5 tiers based on cost, from low to high. In general, the lower the tier number, the lower the cost. Deductibles may vary between tiers.

The infamous "Donut Hole:" The cycle starts over on January 1 each year. The patient pays the full cost of prescriptions up to the deductible (typically $435 this year; some have lower or no deductible), then the plan provides "initial coverage," paying a high percentage of your Rx costs, up to $4020 total drug costs (what you've paid + what they've paid). Then comes the Coverage Gap (Donut Hole), where you pay 25% of the retail price, up to $6350 of total out-of-pocket costs. Then Catastrophic Coverage provides coverage to the end of the calendar year, with your copays being very, very small. Roughly 15% of Medicare beneficiaries nationwide reach the coverage gap stage.

Part D Notes: The amount the insurance company pays for prescriptions depend on the stage, and dollar limits for the stages can change each year. Many people never reach the coverage gap (i.e., if they don't require many prescriptions that year). The patient must be enrolled in Medicare Part A, Part B, or both. May be required to use a pharmacy network. Coverage and costs vary by plan and may change each year. There is a Part D premium penalty for late enrollment. Must enroll within 63 days after qualifying for Medicare to avoid the penalty.

Medicare Supplement Insurance: "Medigap" -- Helps pay some costs not paid by Medicare. It supplements Original Medicare (Part A and Part B). It can't be used with Medicare Advantage. This is an alternative. There are 8 plans with benefits standardized by the federal government. The plans are offered by private insurance companies. The plans may help pay Part A and Part B deductibles; Copays, coinsurance and provider excess charges; Cost for up to an extra 365 days of hospital care after lifetime reserve days are used; Cost of blood transfusions (first 3 pints); and the cost of foreign travel emergency, up to plan limit.

These plans do not help with Prescription drugs; Routine dental, vision or hearing care, eyeglasses, contacts or hearing aids (Some plans may offer special programs to members to help with some of these costs); Extra days in a skilled nursing facility after the Part A benefit is maximized; Custodial care (help bathing, eating, dressing); and Long-term care.

Note: Plans C and F will not be available to persons turning 65 this year. These plans saved patients $198 of deductible for Plan B, which will no longer be allowed, by a 2015 act of congress.

Medigap facts: Must be enrolled in both Medicare Part A and Part B, and live in the state where the plan is offered. There is no medical underwriting requirement, up to 6 months after enrolling in Part B at age 65 or older. Coverage is nationwide, and there is no (restrictive) provider network. It is guaranteed renewable (as long as

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material facts are stated correctly on the application and premiums are paid). Plan premiums may vary, even for the same coverage, between providing insurance companies. Plans with more coverage generally have higher premiums. You must continue to pay the Part B premium to Medicare.

6. How do I choose? Medicare Supplement or Medicare Advantage?

COVERAGE Medicare Supplement: Pays some costs not paid by Original Medicare; Does not help with drug costs; Gives nationwide coverage. Medicare Advantage: Provides benefits of Original Medicare and beyond; Often includes drug coverage; May have a provider network.

COST Medicare Supplement: Monthly plan premium; Drug plan premium and other costs if coverage added; Out-of-pocket costs depend on the plan chosen. Medicare Advantage: May charge a plan premium; Often no additional premium for drug coverage; Copays or coinsurance for most covered services; There is an annual out-of-pocket maximum

CONVENIENCE Medicare Supplement: Multiple plans (when added to Original Medicare along with a Part D plan). Medicare Advantage: All-in-one

7. When can I enroll? The Initial Enrollment Period is from 3 months before, to 3 months after the month in which you turn 65 years old. You would be enrolled in Part A and Part B automatically if receiving Social Security or Railroad Retirement Board (RRB) benefits at age 65, or after receiving Social Security disability benefits for 24 months. Enroll yourself if not receiving such benefits (go to SSA.gov or local office). Enroll early to avoid gaps in coverage and late enrollment penalties! You may refuse or delay enrollment in Part B (penalties may apply later). You may enroll in a Medicare Advantage or a prescription drug plan.

General enrollment periods:

Every year from January thru March, for Parts A & B; April thru June for Parts C & D, for those who miss their Initial Enrollment Period. You may enroll in Part A, Part B or both. You may choose to enroll in a Medicare Advantage plan (Part C) or a prescription drug plan (Part D). Late enrollment premium penalties may apply.

Medicare Supplement Open Enrollment: If you enroll within six months after the month you turn 65, and if you are enrolled in Part B, there is no underwriting (medical/health requirement). You can enroll later, but could be denied or charged more based on your health history. There is no specific late-enrollment penalty, and you can enroll at any time during the year(s).

"Special Enrollment Period:" Working Past Age 65: You have 8 months after the month that you stop working (assuming that you had creditable health coverage from your employer), to enroll in Parts A &/or B; after employment or employer health insurance ends you have up to two full months to enroll in Parts C &/or D without penalty. You must be enrolled in Part A and part B to be eligible for a Medicare Advantage plan. Part B enrollment triggers a six-month open enrollment period for Medicare Supplement (that is, with no health questions).

Late enrollment premium penalties: Part A: No penalty if qualified for "premium free" due to work history; otherwise 10% of the premium amount. Part B: None if qualified for a special enrollment period; otherwise 10% penalty for each 12-month period (e.g., 30% penalty if 3 years delay in enrolling; the penalty applies to all premiums thereafter forever!). Part D: No penalty if less than 63 days without "creditable" coverage (not including COBRA); otherwise 1% of current average premium for each month you are late, forever after.

8. When can I change my coverage? There is open annual enrollment for Medicare each October 15th – December 7th. You can switch from Parts A & B to a Part C plan, or vice versa. Or switch from one Medicare Advantage to another. You can also join, switch or drop your Part D drug plan. Changes take effect Jan. 1 of the following year.

Medicare Advantage Open Enrollment, January through March each year: For Medicare Advantage members only; allows switching to a different Medicare Advantage plan, or returning to Original Medicare. May enroll in a Part D plan and/or a Supplement plan if returning to Original Medicare. Just one coverage change is allowed each year during those three months. If switching to a Supplement plan, health questions apply.

Qualifying Events for the "Special Enrollment Period." This period allows two months after a move or you notify your plan, to enroll in Parts C & D. These events include: Moving out of your plan service area, or within your plan service area but to where there are new plan options; Leaving or losing other health care coverage; Qualifying for a Special Needs Plan (e.g., developing a serious case of diabetes); Moving into or out of an institution, such as a nursing home; Getting or losing financial help with Medicare; or Moving back to the U.S. after living outside the country.

9. How can I save money? Use benefits wisely! Use preventive services (many no-cost services are available). Stay in your plan provider network. Ask about generic and low-tier drugs. Use your plan's preferred or mail-order pharmacy. Understand your status in the hospital

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(outpatient – no coverage; inpatient costs receive coverage).

Financial Assistance Programs: Call your state SHIP (State Health Insurance Assistance Program) office. Visit shiptacenter.org or call 1-800-MEDICARE (1-800-633-4227), TTY 1-877-486-2048, 24 hours a day, 7 days a week to get the number. Extra Help: Helps with drug costs. Medicaid: Provides health care coverage for people and families with limited incomes (e.g. full Medi-Cal Medicare (full dual) individuals under $1,084 monthly income with less than $7,860 in assets other than home and car). Medicare Savings Programs: Help pay Part A and Part B costs. Programs for All-Inclusive Care for the Elderly: Provides care services for frail elderly living in the community.

10. Where can I go for help? Visit MedicareMadeClear.com for more information as well as videos, quizzes, downloadable guides, online tools and more. Sign up for the newsletter on the website and get practical, up-to-date articles delivered to your inbox. Follow on Facebook to stay current with Medicare news. Visit the YouTube page to watch videos on Medicare and health and wellness topics. The MedicareMadeClear.com website can be viewed in English, Spanish, Vietnamese and Chinese.

Get to Know Medicare: September 15–21, 2020, sponsored by United Healthcare and devoted to helping people: Learn about Medicare. Get answers to questions, Feel confident making Medicare decisions. You can participate through local educational events and online activities.

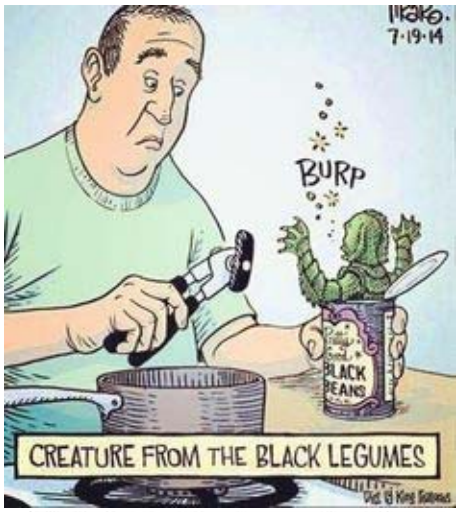
Medicare.gov (24/7); call 1-800-MEDICARE (633-4227) or TTY 1-877-486-2048. Call SHIP (State Health Insurance Assistance Program) – see above. Contact your local Social Security or state Medicaid office.

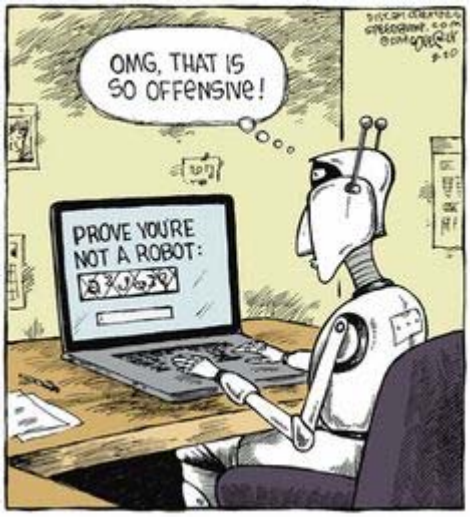
Question: What about the ability to change insurance at a birthday? In your birthday month (if you live in California or Oregon), you can change your Medicare Supplement (Medigap) plan to another provider, or to a different plan offered by your current provider. This does not apply to those with Medicare Advantage.

Contact information: Richard Russell, Phone: 760-214-8715; TTY 711, Email: rarffg@gmail.com

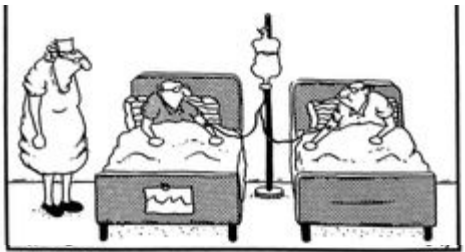
Due to COVID-19, no in-person meetings at the Sanford Burnham Prebys Medical Discovery Institute will take place until further notice. This meeting will be available on DVD.

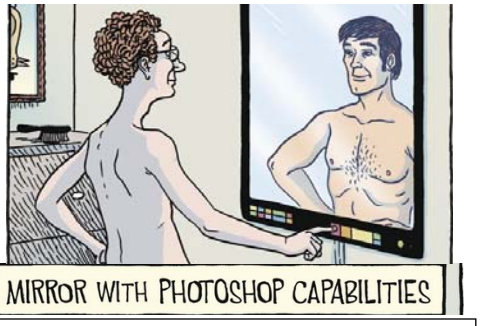
On the lighter side





Me trying to stay sleepy when I go to the bathroom at 4 a.m.





Articles of Interest

Novel insights of how prostate cancer causes secondary tumors

sciencedaily.com

An increased awareness on a molecular level of what mechanisms prostate cancer cells use to become mobile and start spreading may in the long run provide new opportunities for treatment of aggressive prostate cancer. This according to a new study by researchers at Umeå University, Sweden, in collaboration with researchers in Uppsala and Tokyo.

"We can show that one specific amino acid in a signalling molecule plays an important role in mobilising the cancer cells and in that way increase the risk of metastases," says Professor Maréne Landström, Umeå University.

This research has studied the growth factor TGF-β, Transforming Growth Factor Beta, which regulates how cells grow and specialise. Previous studies have shown an overproduction of TGF-β in many cancer forms, one being prostate cancer. High levels of TGF-β have proven to be strongly linked with poor prognosis and low survival rates as a consequence of the growth factor stimulating cancer cells to spread in the human body and cause life-threatening secondary tumors -- so-called metastases.

TGF-β regulates the expression of the protein Smad7 -- an active component in the TGF-β signalling chain. In healthy cells, Smad7 can prevent continued TGF-β signalling via negative feedback. However, Maréne Landström and her research group and colleagues can now show, contrary to previous belief, that, in cancer cells, Smad7 can reinforce the development of tumors by regulating the gene expression of HDAC6 and c-Jun.

The specific amino acid that has caught the researchers' attention is called Lys102 and is found in Smad7. This amino acid binds to particular gene-regulating functions in DNA to increase production of the gene expression HDAC6 and c-Jun. This has the effect that cancer cells become more mobile and more prone to form metastases. Researchers have been able to see a clear connection between all these variables and a negative prognosis for prostate cancer.

"The good news is that by using treatment with an HDAC6 inhibitor, we can make prostate cancer cells lose their mobility. In that way, novel opportunities can open up for treatments that reduce the risk of metastases," says Maréne Landström.

Clinical trials are now taking place in the UK to find specific HDAC6 inhibitors in patients with solid tumors, which means that treatments using HDAC6 inhibitors can become a complement in the cancer treatment of patients with hard-to-treat forms of disease. Future studies can explore the benefit of indicating expressions of Smad7, HDAC6 and c-Jun to enable new and more specific treatments for men with aggressive prostate cancer.

The study also shows an entirely new function of Smad7 in the way that it can recruit Smad2 and Smad3 to the place of transcription for these genes. Previously, it has been thought that Smad7 held the role of inhibitor for TGF beta-Smad2/3 transcriptional activity.

Story Source:

Materials provided by **Umea University**. Original written by Ola Nilsson. *Note: Content may be edited for style and length.*

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'Spare Tire' Increases Prostate Cancer Risk - MedicineNet Health News

medicinenet.com

WEDNESDAY, Sept. 2, 2020

Men: A bulging belly may be bad for more than your heart. A new study suggests it might also up your risk of dying from prostate cancer.

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Researchers analyzed data from more than 218,000 men in Britain who were free of cancer when they enrolled in the U.K. BioBank study between 2006 and 2010.

Over almost 11 years of follow-up, nearly 600 of the men died of prostate cancer. There was no clear association between risk of prostate cancer death and body mass index (BMI -- an estimate of body fat based on weight and height) or total body fat percentage.

However, there was a link between high levels of fat around the belly and waist (central adiposity) and prostate cancer death risk, according to the study being presented this week at the virtual European and International Conference on Obesity.

Men in the top 25% for waist circumference were 35% more likely to die of prostate cancer than men in the bottom 25%, while those in the top 25% for waist-to-hip ratio were 34% more likely to die than men in the bottom 25%.

"We found a significant association between concentration of body fat around the belly and waist and the risk of prostate cancer death, but no clear association between total body fat and risk of prostate cancer death," said study author Aurora Pérez-Cornago, a senior nutritional epidemiologist and Cancer Research UK fellow at the Cancer Epidemiology Unit of the University of Oxford.

"A high BMI increases the risk of other diseases, including other types of cancer, so people should consider the implications of excess body fat wherever it is found in the body," she added in a meeting news release.

"Future work will examine associations between adiposity and aggressive types of prostate cancer, including advanced-stage and high-grade disease," Pérez-Cornago concluded.

-- Robert Preidt

References

SOURCE: European and International Conference on Obesity, news release.

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Delaying RT for Higher-Risk Prostate Cancer Found Safe

Susan London

medscape.com

A study of more than 60,000 prostate cancer patients suggests it is safe to delay radiation therapy (RT) for at least 6 months for localized higher-risk disease being treated with androgen deprivation therapy.

These findings are relevant to oncology care in the COVID-19 era, as the pandemic has complicated delivery of radiation therapy (RT) in several ways, the study authors wrote in JAMA Oncology.

"Daily hospital trips for RT create many possible points of COVID-19 transmission, and patients with cancer are at high risk of COVID-19 mortality," Edward Christopher Dee, a research fellow at Dana-Farber Cancer Institute in Boston, and colleagues wrote.

To assess the safety of delaying RT, the investigators analyzed National Cancer Database data for 63,858 men with localized but unfavorable intermediate-risk, high-risk, or very-high-risk prostate cancer diagnosed during 2004-2014 and managed with external beam RT and androgen deprivation therapy (ADT).

Only 5.6% of patients (n = 3,572) initiated their RT 0-60 days before starting ADT. Another 36.3% (n = 23,207) initiated RT 1-60 days after starting ADT, 47.4% (n = 30,285) initiated RT 61-120 days after starting ADT, and 10.6% (n = 6,794) initiated RT 121-180 days after starting ADT.

The investigators found that 10-year overall survival rates were similar regardless of when patients started RT.

Multivariate analysis in the unfavorable intermediate-risk group showed that, relative to peers who started RT before ADT, men initiating RT later did not have significantly poorer overall survival, regardless of whether RT was initiated 1-60 days after starting ADT (hazard ratio for death, 1.03; *P* = .64), 61-120 days after (HR, 0.95; *P* = .42), or 121-180 days after (HR, 0.99; P = .90).

Findings were similar in the combined high-risk and very-high-risk group, with no significant elevation of mortality risk for patients initiating RT 1-60 days after starting ADT (HR, 1.07; *P* = .12), 61-120 days after (HR, 1.04; *P* = .36), or 121-180 days after (HR, 1.07; *P* = .17).

"These results validate the findings of two prior randomized trials and possibly justify the delay of prostate RT for patients currently receiving ADT until COVID-19 infection rates in the community and hospitals are lower," the authors wrote.

Despite the fairly short follow-up period and other study limitations, "if COVID-19 outbreaks continue to occur sporadically during the coming months to years, these data could allow future flexibility about the timing of RT initiation," the authors concluded.

Experts Weigh In

"Overall, this study is asking a good question given the COVID situation and the fact that many providers are delaying RT due to COVID concerns of patients and providers," Colleen A. Lawton, MD, of the Medical College of Wisconsin, Milwaukee, commented in an interview.

At the same time, Dr. Lawton cautioned about oversimplifying the issue, noting that results of the Radiation

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Therapy Oncology Group (RTOG) 9413 trial suggest important interactions between the anatomic extent of RT and the timing of ADT on outcomes (Int J Radiat Oncol Biol Phys. 2007 Nov 1;69[3]:646-55).

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Quantifying the Number of Cancer Deaths Avoided Due to Improvements in Cancer Survival since the 1980s in the Australian Population, 1985–2014

Paramita Dasgupta, Susanna M. Cramb, Kou Kou, Xue Qin Yu and Peter D. Baade

cebp.aacrjournals.org

DOI: 10.1158/1055-9965.EPI-20-0299 Published September 2020

Abstract

Background: This study quantifies the number of potentially "avoided"cancer deaths due to differences in 10-year relative survival between three time periods, reflecting temporal improvements in cancer diagnostic and/or treatment practices in Australia.

Methods: National population-based cohort of 2,307,565 Australians ages 15 to 89 years, diagnosed with a primary invasive cancer from 1985 to 2014 with mortality follow-up to December 31, 2015. Excess mortality rates and crude probabilities of cancer deaths were estimated using flexible parametric relative survival models. Crude probabilities were then used to calculate "avoided cancer deaths" (reduced number of cancer deaths within 10 years of diagnosis due to survival changes since 1985–1994) for all cancers and 13 leading cancer types.

Results: For each cancer type, excess mortality (in the cancer cohort vs. the expected population mortality) was significantly lower for more recently diagnosed persons. For all cancers combined, the number of "avoided cancer deaths" (vs. 1985–1994) was 4,877 (1995–2004) and 11,385 (2005–2014) among males. Prostate (1995–2004: 2,144; 2005–2014: 5,099) and female breast cancer (1,127 and 2,048) had the highest number of such deaths, whereas <400 were avoided for pancreatic or lung cancers across each period.

Conclusions: Screening and early detection likely contributed to the high number of "avoided cancer deaths" for prostate and female breast cancer, whereas early detection remains difficult for lung and pancreatic cancers, highlighting the need for improved preventive and screening measures.

Impact: Absolute measures such as "avoided cancer deaths" can provide a more tangible estimate of the improvements in cancer survival than standard net survival measures.

Footnotes

Note: Supplementary data for this article are available at Cancer Epidemiology, Biomarkers & Prevention Online (http://cebp.aacrjournals.org/).

Survival following upfront chemotherapy for treatment-naïve metastatic prostate cancer: a real-world retrospective cohort study

Alicia K. Morgans

nature.com

Abstract

Background

Upfront chemotherapy prolongs overall survival for men with metastatic, hormone-sensitive prostate cancer (mHSPC) based on data from clinical trials. We sought to assess the association between upfront chemotherapy and overall survival in men with mHSPC in a real-world cohort.

Methods

We performed a retrospective cohort study of men with de novo, treatment-naïve metastatic prostate cancer from a large, national cancer database in the United States (2014–2015). Men in the upfront chemotherapy group received chemotherapy within 4 months of diagnosis ($n = 1033$, 28%) versus no chemotherapy or chemotherapy later than 12 months after diagnosis (controls; $n = 2704$, 72%). Overall survival was assessed using Kaplan–Meier estimates and compared using multivariable Cox regression analysis.

Results

After a median follow-up of 23 months, median overall survival was 35.7 months in the upfront chemotherapy group and 32.5 months for controls (log-rank $p < 0.001$). After adjusting for patient and clinical variables, upfront chemotherapy was associated with longer overall survival (hazard ratio 0.78, 95% confidence interval 0.68–0.89, $p < 0.001$). In exploratory analyses, the association between upfront chemotherapy and overall survival did not differ by age groups, race, or number of comorbidities (all interaction $p > 0.2$).

Conclusions

In this real-world cohort, *upfront chemotherapy for mHSPC was associated with longer overall survival*. These data support the continued use of chemotherapy for men with mHSPC regardless of race or age if they are fit for chemotherapy and underscore the importance of evaluating cancer therapeutics outside of clinical trials to demonstrate treatment efficacy in populations that may be underrepresented in clinical trials.

Download references

Cite this article

Weiner, A.B., Ko, O.S., Li, E.V. *et al.* Survival following upfront chemotherapy for treatment-naïve metastatic prostate cancer: a real-world retrospective cohort study. *Prostate Cancer Prostatic Dis* (2020). https://doi.org/10.1038/s41391-020-00278-0

Download citation

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Surgery Rates Doubled for High-Risk Prostate Cancer

medpagetoday.com Oncology/Hematology > Prostate Cancer

— Use of prostatectomy nearly equaled radiotherapy in 2016

by Ian Ingram, Deputy Managing Editor, MedPage Today August 31, 2020

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As the rates of high-risk prostate cancer in the U.S. increased in recent years, use of prostatectomy nearly doubled while radiotherapy declined, new research from the National Cancer Database (NCDB) found.

From 2004 to 2016, the proportion of prostate cancer cases classified as high risk increased from 11.8% to 20.4%, and use of prostatectomy in this population rose from 22.8% to 40.5% during this time (*P*<0.001 for both), according to Himanshu Nagar, MD, a radiation oncologist at Weill Cornell Medicine in New York City, and colleagues.

This increase in surgery was met with declines in radiotherapy use for high-risk patients, which fell from 59.7% to 43.3% over this stretch of time (*P*<0.001), the group reported in *JAMA Network Open*.

These shifts in treatment patterns have taken place without guideline evidence suggesting superiority of prostatectomy, Nagar's group noted.

"The increasing use of robotic approaches suggests urologists and patients may regard prostatectomies safer than previous techniques," the authors wrote. "Conversely, a decrease in radiotherapy may reflect reluctance toward recommended androgen deprivation therapy with radiotherapy."

From 2004 to 2013, the likelihood that a patient would receive prostatectomy increased, and then held steady through 2016 (OR 2.34, 95% CI 2.12-2.48, *P*<0.001). This increase was observed regardless of race, though Black men were still less likely to undergo surgery across the study period (OR 0.57, 95% CI 0.55-0.59, *P*<0.001).

Several factors increased the odds of prostatectomy, including higher income and education, treatment at an academic center, and having private insurance. Conversely, higher Gleason score, disease stage, prostate-specific antigen (PSA) levels, and age, as well as living in a rural area all reduced the odds of undergoing surgery.

Radiotherapy and prostatectomy are both standard options for men with high-risk prostate cancer -- defined as clinical stage T3-T4, high Gleason scores (8-10), or PSA levels over 20 ng/mL. Comparisons of the two approaches have shown conflicting results in single-center studies, though some population-based analyses have favored surgery.

A study in Gleason 9-10 tumors showed improved prostate cancer-specific mortality with external-beam radiation therapy (EBRT) plus a brachytherapy boost versus surgery or EBRT alone, but no difference between surgery and EBRT alone. In the current analysis, few patients received a brachytherapy boost.

"Randomized data comparing modalities do not and likely will not exist in the foreseeable future to determine optimal treatment," the authors wrote. "The ProtecT trial compared prostatectomy vs radiotherapy and showed no difference in prostate-cancer specific mortality, but did not include a significant number of patients with high-risk prostate cancer."

Similarly, the ongoing PACE (Prostate Advances in Comparative Evidence) trial is restricted to low- or intermediate-risk prostate cancer.

For their study, Nagar's group examined the treatment for 214,972 men in the NCDB diagnosed with high-risk prostate cancer from 2004 to 2016. More than three-fourths (78%) of the cohort were diagnosed after age 60, with 79.2% white and 16.1% Black. Most men were treated with either prostatectomy (n=104,635) or radiotherapy (n=75,847), with 12.6% receiving EBRT. Gleason score of 4+4 was most common (35%), followed by 4+5 (21.1%), 3+4 (12.2%), and ≤6 (11.2%).

Limitations of the study included its restrospective design.

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Protecting Your Bones and Improving Your Quality of Life During Prostate Cancer Treatment — Cancer ABCs

cancerabcs.org

Should you use Denosumab (Xgeva) instead of Zoledronic Acid (Zometa) to delay skeletal-related events, reduce pain, and improve your quality of life?

Suppose you have castration-resistant prostate cancer (CRPC) with bone metastases (BM). In that case, you are at significant risk of suffering debilitating pain. This pain will impact every aspect of your daily functioning and significantly diminish your quality of life (QoL). There are options to treat this situation. Finding the best drug or treatment to control the pain will allow you to have a more complete and fulfilling life and increase your QoL.

The earlier standard of care for bone health in men in treatment for CRPC was a drug called Zoledronic Acid (Zometa). However, in Phase III clinical trials, the superiority of the drug called Denosumab (Xgeva) over Zoledronic acid (Zometa) has been demonstrated. Xgeva is superior in delaying or preventing the development of skeletal-related events, including pathological fractures.

An ad-hoc analysis, focusing on the subgroup of men with no or mild pain at baseline of this trial, showed that Xgeva is also superior to Zometa for pain interference (PI) and maintaining a better cancer-specific quality of life (QoL).

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The trial showed that over 18 months, more Zometa treated men than Xgeva treated men experienced a more significant worsening of their QoL. In other words, men who used Xgeva had a better quality of life.

Denosumab, which also has shown its ability to delay the initial onset of skeletal-related events, again significantly slowed the time to worsening of pain and allowed men to maintain a better overall QoL

Should you be having Xgeva instead of Zoledronic acid? Speak to your doctor about this question.

Clinical trial information: NCT00321620.

J Clin Oncol 32, 2014 (suppl 4; abstr 12); Donald Patrick, Charles S. Cleeland, Lesley Fallowfield, Matthew Raymond Smith, Laurence Klotz, Stephane Oudard, Gavin M. Marx, Rachel Wei, Katarina Ohrling, Yi Qian

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Abiraterone and enzalutamide had different adverse effects on the cardiovascular system: a systematic review with pairwise and network meta-analyses

Hsiu-Mei Chang

nature.com

Abstract

Background

Abiraterone and enzalutamide may increase the risk of cardiovascular events in patients with castration-resistant prostate cancer (CRPC).

Methods

A comprehensive literature search was performed using a combination of keywords related to "abiraterone," "enzalutamide," "prostate cancer," and "adverse events." Phase II–IV randomized controlled trials (RCTs) on abiraterone or enzalutamide for patients with nonmetastatic or metastatic CRPC were included. Outcome measures included (1) any grade cardiac disorder, (2) severe grade cardiac disorder, (3) any grade hypertension, and (4) severe grade hypertension, as defined by the Common Terminology Criteria for Adverse Events. Pairwise meta-analysis and Bayesian network meta-analyses were performed to investigate the risk ratios (RRs) of abiraterone and enzalutamide. Surface under cumulative ranking curves (SUCRAs) and cumulative ranking probability plots based on the probability of developing cardiac disorders or hypertension were presented.

Results

A total of 7103 patients from seven RCTs were included. Upon pairwise meta-analysis, abiraterone was associated with increased risks of any grade (RR = 1.34, 95% confidence interval (CI) = 1.05–1.73) and severe grade cardiac disorders (RR = 1.71, 95% CI = 1.16–2.53); enzalutamide was associated with increased risks of any grade (RR = 2.66, 95% CI = 1.93–3.66) and severe grade hypertension (RR = 2.79, 95% CI = 1.86–4.18). Based on the SUCRA rankings, *abiraterone had a higher probability of cardiac disorders* (84.84% for any grade and 85.12% for severe grade) than enzalutamide (62.83% for any grade and 50.76% for severe grade); whereas *enzalutamide had a higher probability of hypertension* (99.43% for any grade and 89.71% for severe grade) than abiraterone (49.08% for any grade and 49.37% for severe grade).

Conclusions

Abiraterone and enzalutamide had different adverse effects on the cardiovascular system. We should take this into consideration when we are deciding on the choice of novel hormonal agents for patients with CRPC.

Lee, H.Y., Chen, H., Teoh, J.Y. *et al.* Abiraterone and enzalutamide had different adverse effects on the cardiovascular system: a systematic review with pairwise and network meta-analyses. *Prostate Cancer Prostatic Dis* (2020). https://doi.org/10.1038/s41391-020-00275-3
DOI: https://doi.org/10.1038/s41391-020-00275-3

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Synergy between radiation of metastases and immunotherapy confirmed

prostatecancerinfolink.net

Two clinical trials have now confirmed the abscopal or bystander effect in prostate cancer. These effects occur when cancer cells that are not directly treated are nonetheless killed.

All cancer therapies kill one type of cancer cell or cancer cells in one place. For example, spot radiation only directly kills the targeted cancer, Xofigo only kills actively growing cancer in bone, Lu-177-PSMA only kills cancer that expresses PSMA, ADT only kills cancer that is hormone-sensitive, and docetaxel only kills cancer cells susceptible to death via microtubule stabilization.

When radiation (and chemotherapy) kill cancer cells, the cellular debris is a source of antigens. Dendritic cells learn to use those antigens to activate killer T cells that then seek out and destroy cancer cells elsewhere that express those antigens. The damaged cancer cells also signal a host of other tumor-toxic molecules to form. Radiation-modified cancer cells that escaped direct annihilation become more immune-susceptible too.

Provenge, a dendritic cell boost coupled with immune-stimulatory factors, seems to be a perfect companion to radiation. Based on data from a small, randomized trial at City of Hope, Twardowski et al. reported equivocal results. They irradiated a single metastasis in men with metastatic, castration-resistant prostate cancer (mCRPC). Progression-free survival was 3.7 months among those who received Provenge after SBRT vs. 2.5 months if they received Provenge without SBRT. This outcome did not reach statistical significance (p = 0.06) on this small sample (about 25 in each arm) or with short follow-up.

However, there are conflicting results. Another small trial randomized 32 mCRPC patients to Provenge + Xofigo or Provenge alone. Xofigo (radium-223 chloride) is a radioactive drug that destroys bone metastases. As reported by Marshall et al., after a median follow-up of 5.3 months:

- Median progression-free survival was 10.7 months for the combination vs 3.1 months for Provenge alone.
- The percentage of patients who had a PSA reduction of > 50 percent from baseline was 33 percent for the combination vs 0 percent for Provenge alone
- The percentage of patients who had an alkaline phosphatase reduction of > 30 percent from baseline was 60 percent for the combination vs 7 percent for Provenge alone
- There were no increases in side effects for the combination

It seems that the greater amount of cell-killing from systemic therapy with Xofigo was better able to stimulate an abscopal effect.

But immune stimulation will never be long-lasting. Eventually, the immune system will regard the cancer cell as if it were a normal healthy cell of one's own and will stop attacking it. To continue the attack, a different sort of immune encouragement is required. These "checkpoint blockers" are currently represented by drugs that have been FDA-approved for use in other cancers or for tailored indications: Yervoy (ipilimumab, a CTLA-4 inhibitor, commonly referred to as "ipi") and Keytruda (pembrolizumab, a PD-1 inhibitor). "Ipi"+ radiation for mCRPC has been tried in two pilot tests. In one study, patients were given radiation to only a single bone metastasis followed by ipi or a placebo, but the addition of ipi did not significantly increase survival. In another study, 50 patients were randomly assigned to get ipi + radiation or ipi alone. With short follow-up, both the PSA and the bone metastasis response was good, and about the same for both groups. A larger study of ipi + radiation vs radiation alone in 799 patients showed no effect (except in select sub-groups) after 10 months of follow-up, but…

There was better news after the 799 patients were followed for a longer time. In an update by Fizazi et al., 2.4 years later, ipi ***did*** increase survival in

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mCRPC patients, all of whom already had docetaxel, who received a single dose (8 Gy) of radiotherapy (SBRT) to one or more (up to 5) bone metastases. The effect reversed over time.

- From 0 to 5 months post-SBRT, survival was 49 percent ***worse*** among those who got ipi
- After 5 months post-SBRT, survival was about 33 percent ***better*** among those who got ipi
- At 2 years, survival was 25 percent with ipi vs 17 percent without ipi
- At 5 years, survival was 8 percent with ipi vs 3 percent without ipi
- Ipi drug toxicity caused death in 7 patients
- The effect was no different for those with ≤5 or >5 bone metastases.

It may be that those who died in the first few months were already beyond being helped, and the ipi toxicity harmed rather than helped them. Indeed, the earlier study showed a benefit in those with better function and no visceral metastases at baseline. Ipi alone has been found to have no effect on survival of mCRPC patients, even when used before docetaxel (see this link). SBRT to bone metastases has not been shown to increase survival (but this is the subject of ongoing clinical trials). It is encouraging that the combination has some effect. Adding androgen blockade may enhance the immune effect still further (Antonarakis and Drake), and radiosensitize the tumors.

There are many unanswered questions:

- Will the abscopal/bystander effect be any better in men who are metastatic but still hormone sensitive?
- Is the abscopal/bystander effect maximized with both dendritic cell enhancement and checkpoint blockade, or is the combination too toxic? Does Keytruda work better than Yervoy?
- What is the optimal timing of radiotherapy and immunotherapy? Should Provenge be used before, during, or after radiotherapy?
- For how long is the abscopal/bystander effect sustained?
- Is there still an abscopal/bystander effect when lymph nodes are irradiated?
- Does the abscopal/bystander effect increase with the number of metastases irradiated?

Is there an abscopal/bystander effect with Lu-177-PSMA? (This is the subject of a clinical trial at UCSF.)

- Will a PARP inhibitor further enhance the abscopal/bystander effect?
- Can the abscopal/bystander effect be utilized for rare types of prostate cancer (e.g., neuroendocrine or undifferentiated)?
- Are there any genomics or biomarkers that are predictive or prognostic?

Editorial note: *This commentary was written by Alan Edel for The "New" Prostate Cancder InfoLink.*

Prostate Theranostics - What the Hell? — Cancer ABCs

cancerabcs.org

Theranostics has been around for a while; however, it is a relatively new word in our lexicon for those of us with prostate cancer.

What is Theranostics other than a cool sounding word and a thing that happens in Germany?

The concept behind Theranostics is pretty simple; it is using the same or similar drugs for both diagnosis and therapy. In prostate cancer, theranostics involves using the same radioisotope to identify or diagnose where the prostate cancer is located and also to use it to treat the disease.

ASCO recently provided an educational presentation you might be interested in reviewing, which offers a good description of Theranostics (see it here).

Theranostics has been in medical use in other clinical care areas long before its use in prostate cancer. The treatment of thyroid cancer is one of the oldest examples where the use of the radioisotope radioiodine is common. Radioiodine, which is taken up by the thyroid gland, thus allowing metastases to be visualized in a scan. If you also inject additional radioiodine amounts, it will also be taken up by the thyroid gland, making the thyroid gland "hot" enough to kill the cancer cells.

In prostate cancer, Radium 223, approved in prostate cancer treatment as a treatment known as Xofigo, is a radioisotope that mimics calcium. Like calcium, Xofigo seeks bone, and where there is more bone turnover and remodeling as happens at the site of bone metastases, more Radium 223 accumulates at these sites.

Radium 223 (Xofigo), landing in bone, specifically at the bone metastases, emits alpha particles that will kill cancer cells. The beauty of Xofigo is that alpha particles have a short reach and kill the cancer cells, but will not penetrate and damage the healthy bone marrow.

The hottest new Theranostics topic in prostate cancer is 177Lutetium (177Lu). 177Lu is an isotope that, when bound to PSMA, allows both diagnoses (visualization on a scan) because it emits gamma radiation for detection and high energy beta radiation that can kill cancer cells.

177Lu shows considerable promise for treating prostate cancer, but it is not yet approved for use in most countries. Several completed trials of 177Lu-PSMA have demonstrated that this Theragnostic can increase overall survival in men with progressing castrate-resistant prostate cancer.

For more details on 177Lu-PSMA treatment, this is an excellent recent review from the European Society of Radiology.

There are some ongoing trials of 177Lu-PSMA, which you can find here.

NETWORKING

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

Member and Director, 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

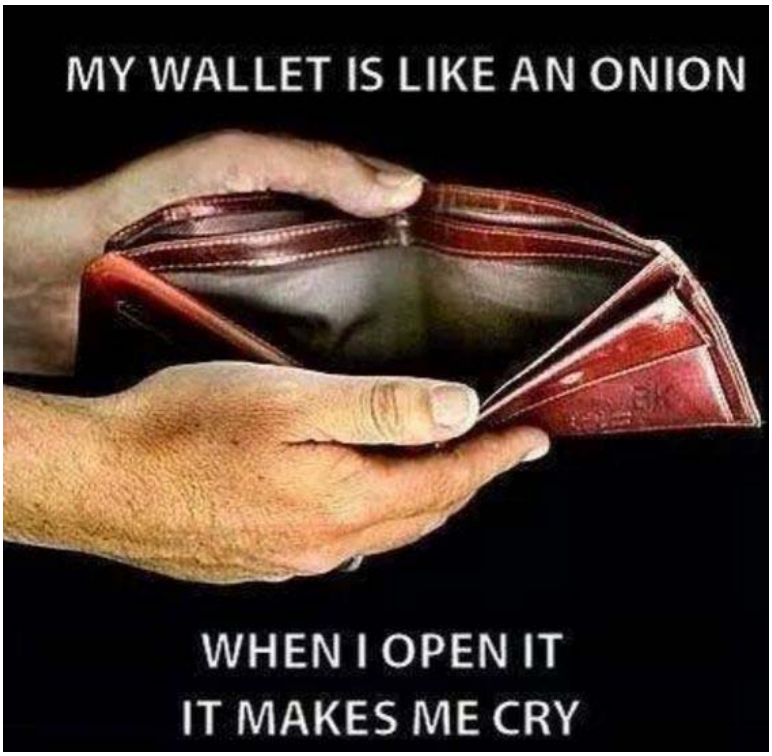
Our brochure provides the group philosophy and explains our goals. Copies may be obtained by mail or email on request. Please pass them along to friends and contacts.

Ads about our Group are in the Union Tribune the week prior to a meeting. Watch for them.

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