

uesday, October 17, 2023

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

**OCTOBER 2023 NEWSLETTER** P.O. Box 420142 San Diego, CA 92142 Phone: 619-890-8447 Web: http://ipcsg.org



Volume 16 Issue 10

## Next Meeting Saturday, October21, 2023 IPCSG-10:00am-Noon PDT.

- Rana R. McKay, MD Novel Therapeutic Strategies for Patients with Advanced Prostate Cancer. Dr. McKay will be highlighting recent FDA approved treatments for advanced prostate cancer. Additionally, she will discuss current novel treatments that are in development and clinical trials of the next generation treatments for prostate cancer. Dr. McKay leads a multi-disciplinary prostate cancer clinic at UCSD focused on delivering advanced cancer care through a coordinated team approach.
- As always, spouses/partners and caregivers are welcome and encouraged to attend!
- After the meeting a light lunch will be served in the foyer outside the meeting room
- For links to further Reading: https://ipcsg.blogspot.com/ (includes member suggested links)
- If you have Comments, Ideas or Questions, email <u>Newsletter@ipcsg.org</u>
- For more information, please send email to bill@ipcsg.org or call Bill at (619) 591-8670 or Gene at (619) 890-8447

# From Drowning in Despair to Swimming in Miracles

### September 2023 IPCSG Presentation - Summary by Bill Lewis

**Dean Hall** is a licensed clinical therapist and coach with over 30 years of experience, an author and highly sought-after speaker, a two-time cancer survivor who experienced radical remission from leukemia and lymphoma, and a two-time world record-setting extreme distance swimmer.

He is the first person in history to swim the entire 187-mile length of Oregon's longest river, the Willamette River (which he did as an active cancer patient) in 2014, and Ireland's longest river, the River Shannon (180 miles), in 2017.

He was raised by adventurous parents in Oregon, climbing, hiking and swimming Alpine lakes and rivers. He chose a small Christian college in Kansas – as if it were a year round religious summer camp – and was disappointed with the terrain, but married and settled down there. He taught school and developed a successful private practice in grief counseling, working 80-hour weeks. Suddenly he was diagnosed with a very serious case of leukemia despite his health-conscious lifestyle. The prognosis was grim: 4-6 weeks (Continued on page 3)

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#### Prostate Cancer: GET THE FACTS



### Organization

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



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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.

## 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 "<u>bill@prostatecancerhelp.info</u>"; or **Director** Gene Van Vleet @ 619-890-8447.

## From the Editor

### In this issue:

Bill Lewis produced a summary of stimulating presentation from the last meeting. For further articles see the blog at <u>https://ipcsg.blogspot.com/</u>. This talk gave some hope in motivating our fight. Many new advanced topics are covered in articles linked in the blog for further reading. Some apparently important optimistic items of interest this month:

- Berbamine targets cancer stem cells and reverses cabazitaxel resistance via inhibiting IGF2BP1 and p-STAT3 in prostate cancer - Wang - if chemo stops working this could restart it.
- 2. .Doublet Therapy Ups Survival in Metastatic Prostate Cancer—use of two therapies at once extends lives
- 3. Decision Making in Prostate Cancer | NEJM—a case is presented, and two panels of doctors present the case for active surveillance versus aggressive treatment. Oncologists vote on the case.

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#### (Continued from page 1)

if things didn't change. He got an excellent oncologist in Oklahoma, but resisted chemo and radiation because of what he had seen his counseling clients suffer. He doubled down on lifestyle changes and got regular blood tests. After a rough year in 2007, he was doing better. With his still-weak immune system, pneumonia in 2008 nearly killed him, but he gradually recovered over the following year.

In 2010, his wife Mary was suddenly diagnosed with an inoperable brain tumor, and passed away within two months, just shy of their 30<sup>th</sup> anniversary. Ironically, Dean was considered a grief expert in the Midwest, but the loss of his wife entirely devastated him. He had married young and was known as "Mary's husband" in their small community where she had long-resident relatives and friends. He became traumatically grief-stricken, and by the following year, his leukemia had come back with a vengeance, bringing with it non-Hodgkins small cell lymphoma. He abandoned his thriving practice, and moved back to Portland, hoping it would be a miracle cure. It wasn't. He no longer had his professional identity and had far fewer friends in Oregon than in Kansas.

Swimming a river in Oklahoma in 2012 to show he had gained strength, gave him viral meningitis and another brush with death. He lost sixty pounds in six days due to the high fever. He couldn't read or think well, and doctors couldn't tell him if he would ever get better. By August 2013, he was down to 152 pounds, and was dying. He considered letting the leukemia/lymphoma take him, but the thought of his daughter losing both her parents gave him pause. Victor Frankl in his book "Man's Search for Meaning" about his experience in Auschwitz described how he found those who survived were not the healthy ones, but the ones tied to a passionate purpose such as seeing loved ones again or fighting the Nazis. Frankl said that the last of our human freedoms is to choose our attitude in any circumstance. He hunted for a personal purpose and passion for weeks. Finally deciding to decorate the apartment he had lived in for six months, the first box he opened had a journal he had been required to write in as an eleven-yearold schoolboy. He had then wanted to climb Mt. Everest and swim the English Channel. An electric shock and goose bumps! Everest was too high, given his health, and expensive. He considered the Channel, and began to swim laps. His lab numbers improved, and he gained some weight. He wanted to inspire other cancer patients, and decided the Channel wasn't unique and meaningful enough. So he chose to swim the entire length of the Willamette river, and surprisingly got sponsored by the leukemia lymphoma society, despite having never done something similar. He had never even been on a swim team. His doctors thought he should wait until he was stronger, even in remission. Never postpone your dreams!

In June 2014, he started to swim the river. It took 22 days, swimming in 40-degree water. He would swim thirty to 45 minutes, jump out and run around to warm up, and get back into the water. For safety, he had to be accompanied by a kayaker. Initial commitments from friends fizzled, then his 79-year-old dad (also a cancer survivor) stepped forward – never having been in a kayak. After a month of practice, away they went, with his mom driving the shuttle van. Initial media coverage was almost non-existent, but when he reached Salem at the 100-mile mark, he began to be noticed.

### Einstein once said that either nothing in life is a miracle, or everything is. Initially resisting the thought, Dean eventually combined this with Frankl's statement about attitude, and credits the two thoughts with his success and recovery.

Dr. Kelly Turner followed Frankl's idea also and studied cancer patients who appeared to spontaneously get better. Of course, it was never spontaneous, but took work and lifestyle changes. The ten lifestyle factors she identified are in her book, Radical Remission, which is in our library. A four-page summary is available from <u>lewis.bill@gmail.com</u>. Dean intuitively followed all of the powerful lifestyle factors Dr. Turner identified, though he only learned of her work later.

Dean shared his personal journey of overcoming cancer and achieving a radical remission by imple-

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Disclaimer IC Information presented herein represents the experience and thoughts of our membership, and should not be any substitute for medical counsel.

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menting various lifestyle changes. He discusses the nine key factors of radical remission, which include changing diet, taking control of one's health, following intuition, using herbs and supplements, releasing suppressed emotions, embracing social support, deepening spiritual practices, and exercising. Dean emphasizes the importance of these factors in his own recovery, such as adopting a clean and organic diet, being proactive in making health decisions, trusting intuition, juicing, allowing for emotional release, finding solace in water, seeking positive emotions through physical activity, and connecting with a supportive community. He also mentions the significance of deepening his spiritual connection and his newfound respect for nature. Dean's inspiring story highlights the transformative power of lifestyle changes in achieving radical remission and living a fulfilling life.

Dean's experience with ice baths and cold water immersion to boost his immune system and achieve a radical remission of leukemia. Dean explains that in preparation for swimming in the Willamette River, which is a snowmelt river with bone-shakingly cold water, he started taking ice baths to acclimate his body to the extreme temperatures. He shares that after swimming the Willamette, a blood test showed that his leukemia was completely gone, defying medical understanding. The constant hypothermic state during his 8-10 hours a day in the river is believed to have boosted his immune system and activated his brown fat stores, which burnout infections. Dean encourages others to consider ice baths or cold plunges as a way to stay healthy and boost their immune system. He also discusses his diet, juicing organic greens and limiting red meat consumption. The speaker shares that many physicians are unwilling to engage in discussions about his remission, and he has faced pushback from some medical professionals.

Changing diet, taking control of your health, following your intuition, using herbs and supplements (especially green juicing – he uses an Omega juicer), releasing suppressed emotions, increasing positive emotions, embracing social support, deepening spiritual connections, and exercise. One day, when you least expect it, the great adventure finds you.

Dean's leukemia is entirely gone, though that is thought to be impossible medically. His doctor believes the cold river water stimulated his immune system. Ice baths and cold-water plunging may boost health, and Dean offers to provide guidance to those who may want to try. In the Q&A, Dean shared what he does to avoid infections from swimming, along with answering other questions.

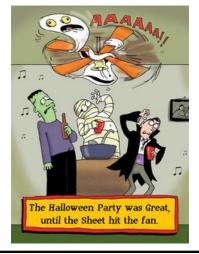
Additional information: Dean's book is <u>The Wild Cure -- From Death to Life on Oregon's Longest</u> <u>River</u>. If you have the Amazon unlimited subscription, it is free to read. For his coaching program and retreats, go to <u>thewildcureway.com</u>.

The <u>video</u> is available on YouTube at https://www.youtube.com/watch?v=NDm86\_9m78Q



On The Lighter Side





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## **Items of Interest**

Berbamine targets cancer stem cells and reverses cabazitaxel resistance via inhibiting IGF2BP1 and p-STAT3 in prostate cancer - Wang - The Prostate - Wiley Online Library

Lili Wang PhD, Chen Lyu MSc, Birgit Stadlbauer, Alexander Buchner, Elfriede Nößner, Heike Pohla

First published: 12 October 2023 https://doi.org/10.1002/pros.24632

### Abstract Background

## Background

Cancer stem cells (CSCs) are a small subpopulation of tumor cells with the capability of self-renewal and drug resistance, leading to tumor progression and disease relapse. Our study aimed to investigate the antitumor effect of berbamine, extracted from berberis amurensis, on prostate CSCs.

### Methods

Sphere formation was used to collect prostate CSCs. The viability, proliferation, invasion, migration, and apoptosis assays were used to evaluate the antitumor effect of berbamine on prostate CSCs. Prostate CSC markers were analyzed by flow cytometry and qRT-PCR. Small RNA sequencing analysis was conducted to analyse miRNAs. Exosomes were extracted using the ExoQuick-TC kit and verified by testing exosomal markers using western blot.

### Results

Berbamine targets prostate CSCs. Additionally, berbamine enhanced the antitumor effect of cabazitaxel, a second-line chemotherapeutic drug for advanced prostate cancer, and re-sensitized Cabazitaxelresistant PCa cells (CabaR-DU145) to cabazitaxel by inhibiting ABCG2, CXCR4, IGF2BP1, and p-STAT3. Berbamine enhanced the expression of let-7 miRNA family and miR-26b and influenced the downstream targets IGF2BP1 and p-STAT3, respectively. Silencing CXCR4 and ABCG2 downregulated the expression of IGF2BP1 and p-STAT3, respectively. Importantly, berbamine enhanced also levels of exosomal let-7 family and miR-26b, suggesting that berbamine possibly influences the expression of let-7 family and miR-26b through exosome delivery. Exosomes derived from berbamine-treated CabaR-DU145 cells re-sensitized the cells to cabazitaxel.

### Conclusion

Berbamine enhanced the toxic activity of cabazitaxel and reversed cabazitaxel resistance potentially through CXCR4/exosomal let-7/IGF2BP1 and ABCG2/exosomal miR-26b/p-STAT3 axes.

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Berbamine and cabazitaxel are two different compounds with potential antitumor effects on prostate cancer, but they work through different mechanisms and have distinct properties.

Cabazitaxel: Cabazitaxel is a chemotherapy drug that belongs to the taxane class of chemotherapeutic agents. It is approved for the treatment of advanced prostate cancer, specifically in cases where other treatments, like docetaxel, have not been effective. Cabazitaxel exerts its antitumor effect by disrupting microtubules within cancer cells, preventing their proper function in cell division and ultimately leading to cell death. It is often used when prostate cancer has become resistant to other treatments, including hormonal therapies.

Berbamine: Berbamine is a natural compound derived from the Berberis plant family and has been studied for its potential anti-cancer properties. While there is some research suggesting that berbamine may have antitumor effects on various cancer types, including prostate cancer, it is important to note that the research in this area is still in its early stages, and more extensive studies

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are needed to establish its effectiveness as a treatment for prostate cancer.

The interaction between berbamine and cabazitaxel specifically in the context of prostate cancer treatment would seem to be shown by this research research and should be verified in clinical trials to show that they have a synergistic effect when used together. The use of combination therapies, including chemotherapy and natural compounds, is an active area of research in the field of cancer treatment.

It's important for individuals with prostate cancer to consult with their healthcare providers, including oncologists, to determine the most appropriate treatment options for their specific case. The choice of treatment will depend on the stage and characteristics of the cancer, as well as the patient's overall health and medical history.

## Doublet Therapy Ups Survival in Metastatic Prostate Cancer

medscape.com

#### Megan Brooks

TOPLINE:

Adoption of doublet therapy — androgen deprivation therapy (ADT) combined with either <u>docetaxel</u> or an androgen receptor pathway inhibitor — has led to a clinically meaningful increase in long-term survival in men with de novo metastatic castration-sensitive <u>prostate cancer</u>, Swedish registry data show.

#### **METHODOLOGY:**

The use of doublet therapy has increased significantly in Sweden in recent years given the growing body of evidence demonstrating that doublet therapy improves survival in individuals with de novo metastatic castration-sensitive prostate cancer.

Investigators wanted to see whether the increasing use of doublet therapy in this patient population has improved survival when taking various other factors into consideration.

The analysis, which included 11,382 men diagnosed with metastatic castration-sensitive prostate cancer in Sweden from 2008-2020 and registered in the country's National Prostate Cancer Register, explored the use of doublet therapy over time and its association with survival, adjusting for age, comorbidities, and cancer characteristics.

The researchers estimated average 5-year and 10-year survival over time using a survival model.

#### TAKEAWAY:

During the study period, patients exhibited a shift toward less <u>advanced prostate cancer</u>, with median prostate-specific antigen (PSA) levels at diagnosis decreasing from 145 to 107 ng/mL in men with metastatic disease.

Upfront treatment with doublet therapy in these men simultaneously increased from 1% in 2016 to 44% in 2020. Adjusted 5-year overall survival increased from 26% between 2008-2012 to 35% in the period 2017-2020; in the 5 years fol-

lowing diagnosis, patients' mean survival increased by about 6 months between 2008-2012 and 2017-2020.

The percentage of patients still alive at 10 years doubled from 9% in 2008 to 18% in 2020. Improvements were greater in men younger than 80 years old.

#### IN PRACTICE:

"A clinically meaningful increase in long-term survival was observed in men diagnosed with de novo [metastatic castration-sensitive prostate cancer] between 2008 and 2020 in Sweden. We argue that the main reason for this improvement was the increased upfront use of doublet therapy," the authors concluded.

#### SOURCE:

The study, with first author Christian Corsini, MD, of Uppsala University in Sweden, was <u>published online</u> October 2 in JAMA Network Open.

Decision Making in Prostate Cancer | NEJM

<u>nejm.org</u>

Freddie C. Hamdy Clinical Decisions

List of authors. Mridula Nadamuni, M.D., Anthony V. D'Amico, M.D., Ph.D., Jenny L. Donovan, Ph.D., F.Med.Sci., and Freddie C. Hamdy,

F.R.C.S.(Urol.), F.Med.Sci.

Case Vignette

A Man with an Elevated PSA Level

Mridula Nadamuni, M.D.

A 61-year-old man with a history of hypertension and obesity establishes primary care with you and requests measurement of his prostate-specific antigen (PSA) level. He reports a family history of prostate cancer; his father received the diagnosis at 67 years of age and died of unrelated causes, and an uncle received the diagnosis at 75 years of age and is still alive. Your patient reports no lower urinary tract symp-

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toms. The physical examination is normal. Records from his previous physician indicate that 5 years earlier, routine laboratory tests were normal; the PSA level was 1.4 ng per milliliter. The patient asks whether he should undergo a digital rectal examination, but you explain that it is no longer recommended for screening. You discuss recommendations from the U.S. Preventive Services Task Force, including the uncertain balance between the potential benefits and harms of prostate cancer screening among men with a family history of prostate cancer, and your patient wishes to proceed with screening. The PSA level is 5.2 ng per milliliter. A urologist performs an ultrasonographic examination and obtains biopsy specimens of the prostate. The prostate volume is 24 cm<sup>3</sup>, and of 12 biopsy cores, 2 show involvement with adenocarcinoma (15% of one and 25% of the other), with a Gleason score of 6, which indicates a low-grade cancer.

The patient is a chemical engineer, enjoys long road trips with his partner of 25 years, and is interested in preserving his sexual function, which is currently normal. He has never smoked, drinks 3 or 4 glasses of wine or beer per week, and exercises occasionally. He schedules a visit with you to discuss the options presented by the urologist and asks your opinion about whether he should pursue radical treatment (prostatectomy or radiation therapy) or should plan for active surveillance.

#### **Treatment Options**

Which one of the following approaches would you take for this patient? Base your choice on the literature, your own experience, published guidelines, and other information.

Recommend radical treatment.

Recommend active surveillance.

To aid in your decision making, we asked experts in the field to summarize the evidence in favor of approaches assigned by the editors. Given your knowledge of the patient and the points made by the experts, which approach would you choose?

Option I: Recommend Radical Treatment Option 2: Recommend Active Surveillance Option I Option 2

#### **Recommend Radical Treatment**

#### Anthony V. D'Amico, M.D., Ph.D.

The Prostate Testing for Cancer Treatment (ProtecT) trial<sup>1</sup> provides data that are relevant to this clinical question. Patients with earlystage, localized prostate cancer were randomly assigned to one of three initial treatment approaches: active monitoring with serum PSA (active-monitoring group), open radical prostatectomy (prostatectomy group), or three-dimensional conformal external-beam radiotherapy and short-course testosterone-lowering therapy or hormonal therapy (radiotherapy group). The primary outcome was prostate cancer– specific mortality; metastasis was a secondary outcome. After a median follow-up of 15 years (range, 11 to 21), prostate cancer–specific mortality was higher in the active-monitoring group (3.1%) than in the prostatectomy group (2.2%) and radiotherapy group (2.9%), but the differences were not significant; however, the percentage of patients with metastasis in the active-monitoring group was twice that seen in the other two groups (9.4% vs. 4.7% and 5.0%, respectively).

A 61-year-old nonsmoker, with controlled hypertension and obesity, has a remaining life expectancy of approximately 20 years,<sup>2</sup> and prostate cancer with a Gleason score of 6 is generally considered to have a slow rate of progression. However, prostate cancer can vary in grade at different sites in the prostate, and the systematic biopsy approach may miss localized lesions with a higher histologic grade. In a randomized trial,<sup>3</sup> patients were assigned to undergo 12-core, transrectal ultrasonography–guided systematic biopsy, targeted biopsies of multiparametric magnetic resonance imaging (MRI)–defined lesions, or both 12-core systematic and targeted multiparametric MRI biopsies to detect prostate cancer. The results showed that more aggressive prostate cancer (Gleason score 3+4 or higher at the time of radical prostatectomy) was detected in 30.2% of men with a Gleason score of 6 on the basis of the 12-core systematic biopsy, as compared with just 6.7% of men who had both 12-core systematic biopsy and targeted multiparametric MRI–guided biopsies. Therefore, a patient with a Gleason score of 6 after systematic biopsy has a 30% chance of having more aggressive prostate cancer.

PSA density — calculated as the PSA level (in ng per milliliter) divided by the prostate volume (in cm<sup>3</sup>) is a known risk factor for adverse pathological findings at the time of radical prostatectomy in patients with a biopsy Gleason score of 6.<sup>4</sup> PSA density is considered to be low-risk if it is less than 0.15 ng per milliliter per cubic centimeter. This patient's PSA density is elevated, at 0.22 ng per milliliter per cubic centimeter (5.2 ng per milliliter/24 cm<sup>3</sup>). The PSA level here has nearly doubled twice in the past 5 years, increasing by 3.8 ng per milliliter, from 1.4 to 5.2, which suggests a PSA doubling time of 2.5 years. Assuming that all potential confounding causes of a falsely elevated PSA level, such as inflammation, infection, instrumentation, ejaculation, recent bike-riding, and constipation, have been eliminated before testing, high-risk PSA velocity would seem not to apply here unless the rate of the rise has accelerated recently. Specifically, an increase in the PSA level of more than 2 ng per milliliter during the year before diagnosis has been shown to be associated with a higher risk of adverse pathological findings at the time of radical prostatectomy, in addition to higher rates of prostate cancer—specific mortality and all-cause mortality after local therapy.<sup>5</sup> This man will need more frequent PSA measurements to be sure that the PSA velocity is not a risk factor. In addition, less than 1% of patients in the ProtecT trial<sup>1</sup> were of African ancestry, and, as a result, the study findings may not apply to this man if he is Black. Enhancing the diversity of patients enrolled in randomized trials of treatment for prostate cancer is urgently needed, given the more aggressive disease at presentation and higher rates of death from prostate cancer in Black patients than in White and Asian patients.<sup>6</sup>

Therefore, before making a treatment recommendation, I would recommend obtaining a multiparametric MRI scan and performing targeted biopsies directed at suspicious areas to more reliably define the Gleason grade of his tumor and assess PSA velocity and density. If additional biopsies yield higher-grade disease or the PSA velocity is found to be increasing rapidly, definitive local therapy may be indicated.

At first glance, one may consider a difference of 1 percentage point in prostate cancer–specific mortality and a difference of 5 percent-(Continued on page 8)

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age points in the incidence of metastasis to be inconsequential, given the potential life-altering side effects from treatment with radical prostatectomy or testosterone-lowering or hormonal therapy. However, the individual patient's wishes, remaining life expectancy, and risk of progression to metastasis and death from prostate cancer are important to consider when making a treatment recommendation. Moreover, modern approaches that use robotic assistance for radical prostatectomy or intensity-modulated testosterone-lowering therapy have the potential to offer improved patient-reported side-effect profiles,<sup>7</sup> since technology has improved since the ProtecT trial was conducted, and definitive therapy may offer patients peace of mind.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

### Recommend Active Surveillance

Jenny L. Donovan, Ph.D., F.Med.Sci., Freddie C. Hamdy, F.R.C.S.(Urol.), F.Med.Sci.

The information provided about this patient suggests that he should consider opting for active surveillance, which requires regular monitoring with PSA tests and MRI, with targeted biopsies performed as necessary to identify adverse changes in time for prompt radical treatment if or when needed. This approach aims to enable patients with clinically localized prostate cancer that has a low risk of lethality to avoid or defer radical treatments and the associated risks of urinary, sexual, and bowel side effects.

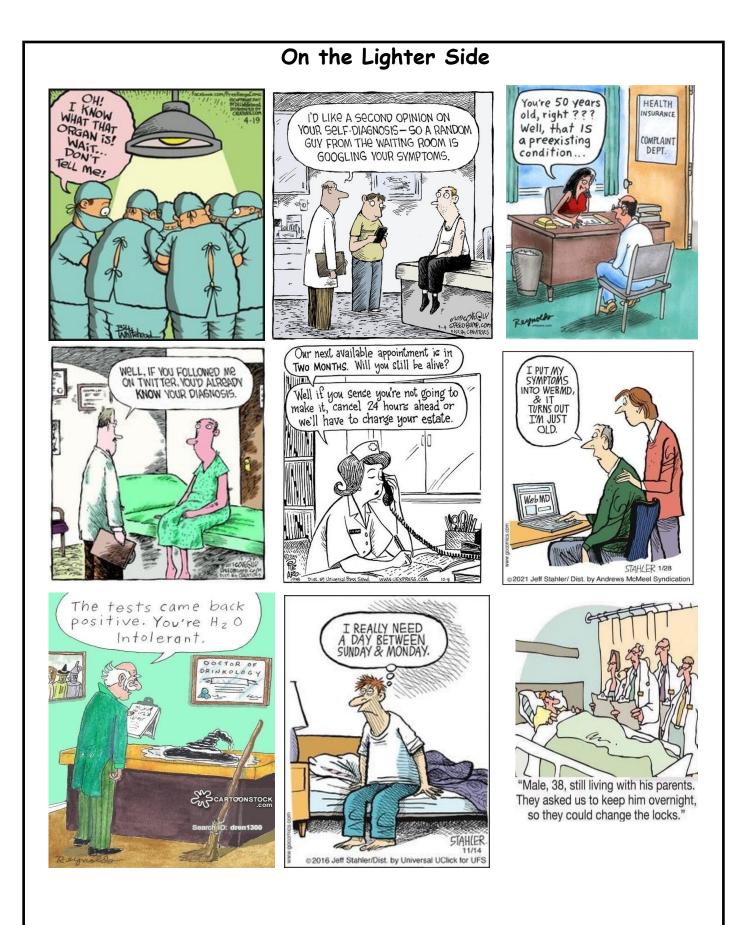
The ProtecT trial showed that men who received a diagnosis of clinically localized prostate cancer after PSA testing and transrectal ultrasonography–guided biopsies had a very low (2 to 3%) risk of prostate cancer–specific death after a 15-year median follow-up, whether they were assigned to active monitoring (a form of active surveillance), radical prostatectomy, or external-beam radiotherapy with neoadjuvant androgen-deprivation therapy.<sup>1</sup> A greater risk of metastases after active monitoring (9%, as compared with 5% with radical treatments) was noted, as were increased risks of urinary leakage and erectile dysfunction after prostatectomy and bowel and sexual effects from radiotherapy over 12 years.<sup>8</sup> The ProtecT trial showed that 24% of men were wearing one pad or more per day for urinary leakage by year 12 in the prostatectomy group, as compared with 11% in the active-monitoring group and 8% in the radiotherapy group. Sexual function was retained most and longest in the active-monitoring group. Bowel function was a little worse in the radiotherapy group. Overall quality-of-life measures showed similar trends.

This patient's apparent low-risk (Gleason score 3+3=6; grade group 1), low-volume prostate cancer and his coexisting conditions, relatively young age, and keenness to preserve his current lifestyle and good sexual function all suggest that active surveillance would be appropriate. However, additional information is required before this option can be selected. First, a comprehensive family history should be obtained, including female relatives with breast or ovarian cancer, in addition to male relatives with prostate cancer, since genetic counseling and testing for *BRCA1* and *BRCA2* gene mutations might be needed.<sup>9</sup> Second, there is a risk that this patient's tumor was undersampled. MRItargeted biopsy identified 12% more participants with clinically significant prostate cancer than transrectal ultrasonography–guided biopsies in the PRECISION trial.<sup>10</sup> Furthermore, in the ProtecT trial, tumor assessments in 30% of men were revised to a higher grade and stage after prostatectomy was performed within 12 months (regardless of the group to which the men had been assigned).<sup>1</sup> Therefore, this patient needs further imaging with multiparametric MRI, followed by targeted biopsies in the presence of visible abnormalities according to the Prostate Imaging Reporting and Data System, possibly with transperineal biopsies performed depending on the anatomical location of the lesions.

If the additional information indicates no genetic abnormalities and confirms that this patient has low-risk cancer (Gleason score 3+3=6; grade group 1), guidelines in the United States<sup>11</sup> and internationally recommend active surveillance, since radical treatments do not improve survival, treatment side effects are avoided with active surveillance, and surveillance methods can help to identify disease progression in time for radical treatment if or when it is needed.<sup>12</sup> These same guidelines advise that active surveillance should be discussed with patients who have favorable intermediate-risk cancer (Gleason score 3+4=7; grade group 2). Since one third of the participants in the ProtecT trial had intermediate-risk cancer, the results of the trial are relevant. In this case, the patient would need to balance his wish to avoid the side effects of radical treatment against an additional risk of cancer progression. Although guidelines do not currently recommend active surveillance for patients with unfavorable intermediate-risk cancer (Gleason score 4+3=7; grade group 3), it may be a preferred initial option if this patient wishes to retain his current lifestyle and sexual function for as long as possible and is prepared to accept additional risks of progression and potentially miss the "window of curability."

This patient's lifestyle priorities need to be included in his treatment decision to avoid later feelings of regret.<sup>13</sup> Whether his cancer is low-risk or is regraded as intermediate-risk, he can consider opting for active surveillance. The ProtecT trial shows that he can take time to carefully weigh the crucial trade-offs between the risks of cancer progression and the side effects of radical treatments, knowing that he has a low risk of dying from prostate cancer within 15 years.<sup>1,8</sup>

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.



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### NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet and Bill Lewis is available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org or Bill 619-591-8670 (<u>bill@prostatecancerhelp.info</u>) 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

### **FINANCES**

We want to thank those of you who have made <u>special donations</u> to IPCSG. Remember that your gifts are <u>tax deductible</u> 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. <u>Corporate donors are welcome!</u>

