“Treating My Osteoporosis and My Prostate Cancer” (Jeff Dwyer) [#65]

Jeff Dwyer, Allen Morris, Brad Power, Paul Van Camp
July 26, 2023

“Unfortunately, I have a bad habit: I don't listen to anybody. I keep asking questions.” – Jeff Dwyer

“I’d written … a real letter, not a digital communication. Nobody receives a real letter any more, so they’ll open it and hopefully read it and respond.” – Jeff Dwyer

“I had been investigating radiation treatment options using proton beam therapy because I had read a lot about it, and it sounded like a wise option if I could find a provider… I selected my radiation oncologist, and I … contacted the … facility myself.” – Jeff Dwyer

Meeting Summary

Jeff Dwyer is facing complex decisions about additional treatment for his advanced prostate cancer following his second prostate cancer recurrence, signaled by an uptick in his PSA (Prostate Specific Antigen, a blood test that monitors his prostate cancer progression). Jeff's decision is complicated as he trades off choices of treatments for his prostate cancer and treatments for his bone disease and heart disease. The most likely course of treatment for his prostate cancer, androgen deprivation therapy, has negative side effects for bone strength and muscle strength (like the heart). Jeff has resisted taking drugs for bone strength due to his research on the side effects. But Jeff has been encouraged by his primary care physician to begin taking drugs to address his osteoporosis -- the bone disease that develops when bone mineral density and bone mass decreases, increasing the risk of bone fractures.

What are Jeff’s best treatment options that can thread the needle between suppressing his prostate cancer and treating his bone and heart disease?

Who is Jeff Dwyer?

Jeff Dwyer is a 76-year-old former literary agent and owner of a bookstore. He leans into researching his treatment decisions. He surveys the medical literature and reaches out to researchers for advice on his course of treatment. He has gone far afield to find the best experts and the best treatments, and he has traveled several times across the country for testing and treatment. He lives with his wife in Northampton, Massachusetts, next to the Amherst colleges.

What is Jeff's medical history?

Jeff was diagnosed with aggressive, Stage 4 (metastatic) prostate cancer in May 2019. (His Gleason scores were 9/10, indicating a high grade, very aggressive cancer). He had a robotic radical prostatectomy in September 2019 at Mass General Brigham, followed by coronary arterial bypass surgery at Mass General Brigham in July 2021. He had a recurrence of his prostate cancer in May 2022, signaled by an uptick in his PSA (a blood test for prostate specific

antigen). He received 34 proton beam sessions of stereotactic radiotherapy (radiotherapy from many different angles on the tumor) at the University of Pennsylvania in September 2022. His PSA was 4.9 after doubling when he began treatment in 2019, and his first prostate cancer recurrence following a PSA of 0.21. His PSA went to undetectable then began to rise again.

Now his second prostate cancer recurrence has occurred with a PSA of 0.21. A PSMA PET CT scan (prostate-specific membrane antigen positron emission tomography scan, an imaging test used to detect prostate cancer throughout the body) at Dana Farber in May 2021 revealed a small bone metastasis (cancer tumor away from the initial site) on his sacrum, a shield-shaped bony structure that is located at the base of the lumbar vertebrae and that is connected to the pelvis. During stereotactic radiotherapy at UPenn, the radiation oncologist treated the bone met and also his prostate bed and lower spinal area. An MRI (magnetic resonance imaging) at UPenn following the stereotactic radiotherapy in October 2022 showed that the bone met was no longer present.

Jeff's medical treatment is complicated by coronary artery disease and congestive heart failure, which caused him to have quintuple coronary artery bypass surgery two years ago.

Jeff's lower back pain led to a DEXA scan (an imaging test that measures bone density and strength), and a follow-up computed tomography (CT) scan and MRI of his spine at Mass General Brigham's Spinal Center, and consultation with an orthopedic surgeon. Jeff found out that he has bone density loss. He has five spinal compression fractures. The orthopedic surgeon recommended no intervention since four of Jeff's five older compression fractures had healed. The orthopedic surgeon predicted that Jeff's recent fifth compression fracture would heal eventually. Jeff has been doing physical therapy and weight training exercises and taking pain medications. He is seeing some progress. The orthopedic surgeon recommended consultation with an endocrinologist because of Jeff's advanced prostate cancer.

Jeff has been updating his dental work in anticipation of the side effects of weakening of his bone strength from hormone therapy. He has had numerous crowns done over the years. Recently he discovered decay below five crowns following gum recession. Because removal of the crowns and the decay below was deep, and the work caused root inflammation and a lot of pain, he's had two root canals following three of the five crown and decay removals. He has one tooth remaining to be processed. He had the extraction and implant work done at the Tufts faculty care practice in Boston. The dental work should finish by September.

What should Jeff do next?

Jeff expects that his oncologist will order a PSMA PET CT scan soon and recommend that he begin some form of hormone therapy to address his recent prostate cancer recurrence. (Hormone therapy for prostate cancer is any treatment that blocks testosterone production or action.) Thus far, he has had no hormone therapy because of the cardiac side effects, but he may need to risk the cardiac side effects to arrest the prostate cancer progression.

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Jeff is researching hormone therapy alternatives now. Jeff's Dana Farber oncologist referred Jeff to an endocrinologist. (Endocrinologists specialize in helping men undergoing androgen deprivation therapy for prostate cancer to monitor for any potential long-term side effects and treat any side-effects early to maximize quality of life and maintain general health.) Jeff is considering estrogen (tE2) for his androgen deprivation therapy (ADT), eventually morphing into bipolar androgen therapy when the tE2 ADT fails. He would be avoiding the other hormone therapy drugs and their bone weakening side effects by using tE2, which improves bone strength, even though it may not be as effective as other ADT for suppression of prostate cancer. This program would be self-administered, non-standard of care, so he doubts that he will find any support at Dana Farber from his medical oncologist or endocrinologist. This is a pending open question for him.

When Jeff asked his radiation oncologist at UPenn what she suggested that he should do if his prostate cancer returned, she suggested that he should return to UPenn for further proton beam radiotherapy of any recurring mets. So radiation plus hormone therapy are a likely next treatment.

Discussion

Jeff engaged in an email conversation with pathologist and advanced prostate cancer survivor Dr. Allen Morris about his case, which clarified some fundamental points for thinking about his testing and treatment, especially whether he had had a recurrence and how big of a recurrence it was, i.e., how aggressive his prostate cancer is. This has a big influence on how much he needs to focus on treating his prostate cancer vs. treating his bone and heart issues. If he has a recurrence, then he needs to go get some prostate cancer drugs like androgen deprivation therapy. But if Jeff hasn’t had a recurrence yet, he doesn’t need to get any prostate cancer treatment at this moment. He can worry about his bones and heart.

- **The “Gleason score" becomes less useful over time to measure the aggressiveness of your cancer; better are “Time to biochemical recurrence (BCR)” and “PSA doubling time”**. As a pathologist, Dr. Morris respects the Gleason score as the measure of prostate cancer aggressiveness. The Gleason score is calculated at initial (core biopsy) diagnosis and at prostatectomy. The Decipher test, just recently FDA approved, and the CAPRA score improve slightly on the Gleason score. The Decipher test looks at the activity of 22 genes in prostate tumors and calculates a score from 0 to 1. The Cancer of the Prostate Risk Assessment (UCSF-CAPRA) test, with a 0 to 10 score, predicts an individual's likelihood of metastasis, cancer-specific mortality, and overall mortality. The score is calculated using points assigned to: age at diagnosis, PSA at diagnosis, Gleason score of the biopsy, clinical stage and percent of biopsy cores involved with cancer. However, as soon as you get to biochemical recurrence (BCR), Gleason is only one of many measures, and not the best, but the possibly the third best, after “Time to biochemical recurrence (BCR)”, and “PSA doubling time”. As you go further in your journey, your Gleason score means less and less, for many reasons.

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- In fact, metastatic prostate cancer is not even Gleason scored. For those PCL patients who have had a metastasis biopsied was the metastasis Gleason scored?
- **What is Jeff’s “Time to BCR” and “PSA doubling time”?** To calculate Jeff’s PSA doubling time, he needs all of his PSA data points over time before his salvage proton radiotherapy for his first biochemical recurrence (BCR), and then all his PSA data points for his second BCR. However, for Jeff there is one huge caveat: almost all of the literature on PSA doubling time is calculated with PSA data points starting at 0.2 and higher, but Jeff’s values are less than 0.2. So his PSA doubling time is not validated and imperfect, but still a worthwhile approximation. Was the first BCR PSA Doubling Time the same, more, or less than his second BCR PSA Doubling Time? Jeff’s Time to BCR of two years and eight months missed the low-risk category by only four months.
- **What is the aggressiveness of Jeff’s cancer?** Jeff’s cancer seems like it is not highly aggressive, but more intermediate. Allen Morris believes Jeff is a good, not bad intermediate risk, which would correspond in Gleason language to Grade Group 2.5.
- **What does this risk assessment mean for Jeff’s treatment?** Jeff’s cancer’s intermediate aggressiveness assessment influences how aggressively he should be in treating his prostate cancer. For example, if Jeff’s “Time to BCR” is greater than three years, and his PSA doubling time is greater than 15 months, he should do "active surveillance" of BCR, and focus on his heart and bone issues. For all the large patient cohort studies, Jeff’s prognosis is probably better than average. Of course, this will be adjusted as soon as the next shoe drops.

Key Take-Aways from the Conversation

Jeff reviewed his case with about 25 participants. Key suggestions for Jeff from the discussion included:

- Get a PSMA PET scan to see where your cancer is.
- Get a liquid biopsy to see if you have any genomic mutations.
- Select a bone mineral density medication and get started.
- Before you start androgen deprivation therapy, make sure any dental work that you need done is taken care of, and that you have excellent oral hygiene.
- Get radiation to your chest before you start hormone therapy to avoid gynecomastia (development of the breast).
- Consult with Dr. Alicia Morgans and Dr. Vivek Narayan on whether an androgen receptor inhibitor (such as apalutamide, darolutamide, or abiraterone) might help and avoid cardiac issues.
- Consider taking Xgeva (denosumab), to treat osteoporosis and bone problems.
- Consider transdermal estrogen therapy for androgen deprivation therapy, which may also decrease the rate of bone decay and reduce cardiac issues.
- Consider bipolar androgen therapy, which can control prostate cancer and increase bone density.
- Consider anabolic steroids, such as nandrolone, to increase bone density.

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Email advice after the discussion from Dr. Paul Van Camp, prostate cancer survivor:

- Agree with the bone plan (Xgeva every three months), and that androgen deprivation therapy can wait for now.
- Would put more focus on the heart disease as that is likely the biggest mortality risk in the intermediate term. Get a full updated lipid profile including ApoB. (ApoB is the main protein found in the low-density lipoproteins - LDL. LDL cholesterol is known as "bad" cholesterol because high levels of it can damage your heart and arteries. The ApoB test helps your healthcare provider figure out your risk for cardiovascular disease.) Discuss with your cardiologist adding a PCSK4 inhibitor (Proprotein convertase subtilisin/kexin type 4 is a crucial enzyme for reproduction, and inhibition may block a pathway to cancer.) to the maximum tolerated dose of statin (Repatha or Praluent). Try to get ApoB and LDL cholesterol down very low, to near 30 to stabilize and possibly reverse ASCV (atherosclerotic cardiovascular disease) plaques. Another path is low dose Colchicine 0.3-0.5mg per LoDoCo study. Reduces major cardiovascular events or death by 31% over two years. Amazing, but must reduce statin dose when starting it, then re-titrate per lipids. Baby ASA (aspirin) too.

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Meeting Notes

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Discussion Outline

1. Introduction to today's session. (0:00)
2. Doctor’s response to request for treatment. (8:58)
3. Hormone therapy for prostate cancer. (15:36)
4. Risks and benefits of preoperative radiation. (23:34)
5. Personal experience with osteoporosis. (31:57)
6. Transdermal estrogen therapy and bone density. (33:45)
7. How do you measure the aggressiveness of your cancer? (37:25)
8. The biochemical recurrence chart. (42:12)
9. The pros and cons of getting a PSMA PET scan. (48:16)
10. The PSA level and PSMA PET scan. (50:32)
11. Can you get genetic testing? (55:28)

SUMMARY KEYWORDS

PSA, bone density, jeff, prostate cancer, morgan, radiation, metastasis, osteoporosis, scan, doctor, rick, psm, cancer, bone, years, estrogen, medical oncologist, point, talking, feel

SPEAKERS

Jeffrey Dwyer (50%), Russ Hollyer (17%), Rick Davis (14%), Brian McCloskey (6%), Robert Gurmankin (6%), David Plunkett (3%), Brad Power (3%), Rick Stanton (2%)

Meeting Transcript

Brian McCloskey
Welcome everybody to the Cancer Patient Lab/Prostate Cancer Lab. We're excited to have this session today. We have a special guest. He's one of the illustrious members of our community, Jeff Dwyer. Jeff is facing a decision in his treatment. He really needs some help to navigate this. What we don't talk about often in our sessions are the comorbidities that patients face. He has a unique situation where he's trying to navigate not only his prostate cancer, but also challenges with his heart as well as bone disease. And so, Jeff is going to talk a little bit about his cancer journey, and tee us up for hopefully a really productive and helpful conversation that can help guide his next treatment decisions. This is what the Cancer Patient Lab/Prostate Cancer Lab is all about. It's helping us as patients make those really important complex decisions as we go through this journey.

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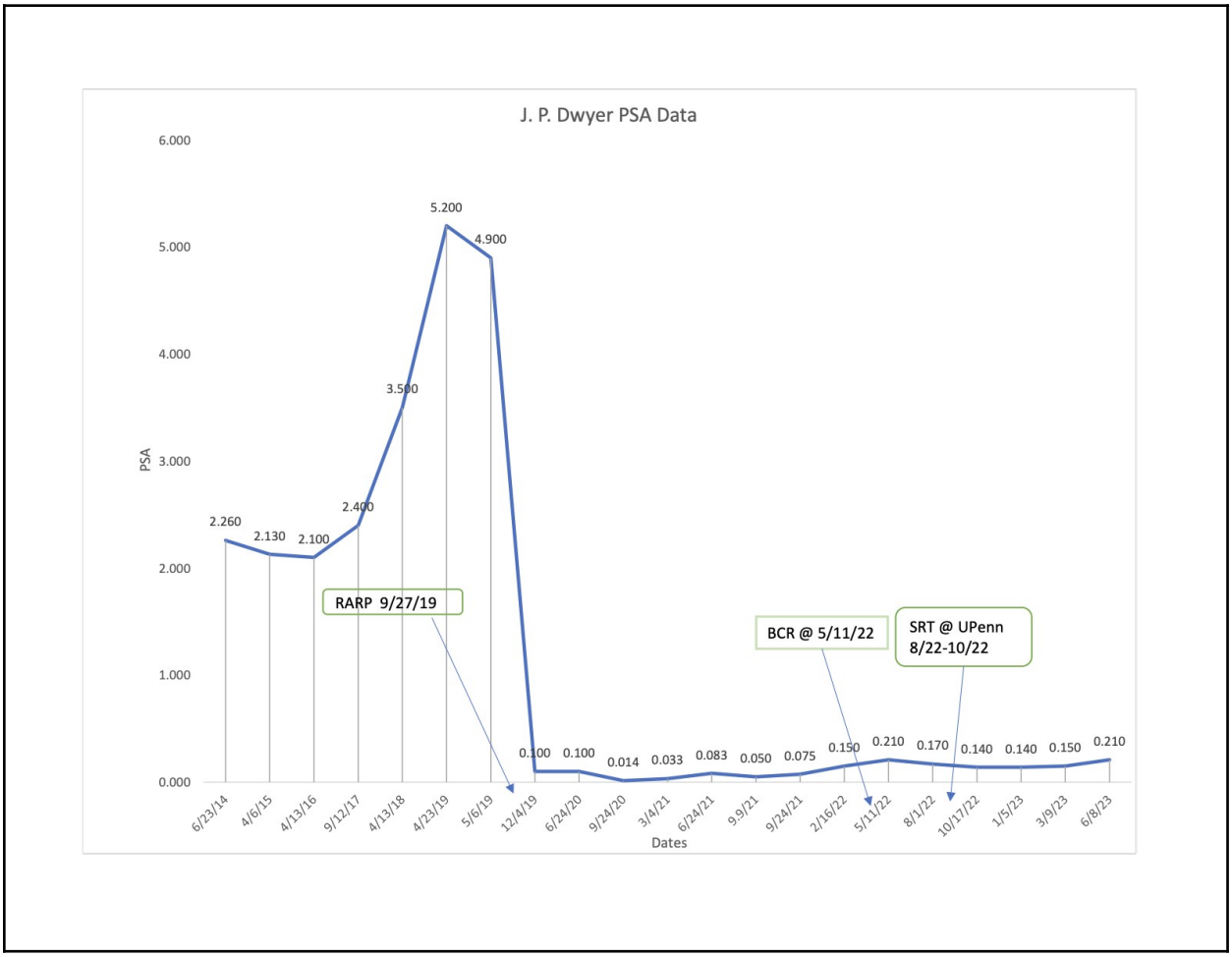
Jeffrey Dwyer 3:04
I was diagnosed with prostate cancer in May of 2019. I was down at our home in Florida at that time, and I returned to Massachusetts. I got a biopsy in August of 2019 at Massachusett General Brigham (MGB) Hospital in Boston. Following the fusion biopsy, I met with a group of docs at MGB composed of a urologist, a radiologist, and a medical oncologist. By that time, I’d read a couple of books about prostate cancer and talked with a group of friends of mine who had the disease and had been dealing with it for several years. When I received the Gleason 9/10 designation, I decided to have a prostatectomy. I had the surgery done at MGB on 9/24/19, and all went well. I got my continence back in about three or four months. And then I waited and watched as my PSA began as undetectable but slowly began to rise.



Jeffrey Dwyer 4:24
By May of 2022, my PSA had risen to 0.21. By that time, I had left MGB and moved over to Dana Farber (DFCI). I had engaged Dr. Alicia Morgans as my medical oncologist (MO). I'd never selected an MO at MGB. I’d written Dr. Morgans a real letter, not a digital communication. Nobody receives a real letter any more, so they’ll open it and hopefully read it and respond. I asked for a consultation, and she agreed. We got along, and she ordered genetics, blood tests and a PSMA PET scan.

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Back in June 2021, at a video session on the patient portal AnCan, I learned of a randomized clinical trial at the Veterans Administration Hospital in Los Angeles. I telephoned the radiologist who was running the trial, and he encouraged me to join the trial even though my PSA was under 0.20. He told me that he had given PSMA PET CT scans to several patients with a PSA below 0.2, and they had mets revealed by the scan. I flew to LA on a red-eye flight, spent two days in a hotel that was walking distance from the VA, and got the PSMA PET CT scan. Because I was a vet, there was no cost for that PSMA PET CT scan. I had no uptake revealed from the scan except for a small spot in my urethra. That was attributed to some of the dye in my urine. So, when I returned to the east coast, I had a PSMA PET CT baseline completed by the VA six months prior to the FDA approving the scans for general use.

The next month, 7/21, I had a cardiac PET scan at MGB. That scan revealed that my heart was in trouble. My ejection fraction (the amount of blood that your heart pumps each time it beats) had diminished, and Dr. Ron Blankstein, my cardiologist, told me that our time together trying to avoid interventional cardiac procedures had reached an unfortunate conclusion.I I needed by-pass surgery - and soon. I returned to MGB and had quintuple cardiac bypass surgery (CABG5) on 7/24/21.

This occurred in the middle of the summer lull of pandemic infections in Boston. I spent twelve days in MGB, and I was sent home for home cardiac-rehab. That was a difficult time for me. I had not expected the impact that the surgery had on me. We resisted home cardiac rehab care because we didn’t want visiting nurses coming into the house for an hour of rehab after leaving someone else’s home just before they arrived at our place. So, I did the rehab myself, and as you would expect, I did not do a great job. I bought a treadmill, and began trying to rebuild some strength.

Fast forward to the spring of 2022 when I contacted Dr. Morgans, consulted with her, and had our first meetings. During my cardiac rehab time, I had researched radiation treatment options. I had always assumed that my prostate cancer (PCa) would recur, and I assumed that my next step would be salvage radiation therapy (SRT). I had resisted taking any hormone treatments (HT) following the robot-assisted radical prostatectomy (RARP) at MGB because I was fearful of the side-effects (SEs) that the HT drugs might have on my heart. Normally, when urology physicians learned of my cardiac issues, they didn’t push HT on me.

Jeffrey Dwyer 8:03
I had been investigating radiation treatment options using proton beam therapy (PBT) because I had read a lot about it, and it sounded like a wise option if I could find a provider. I had telemedicine conferences with Dr. Randal Cunningham at the University of Florida Proton Beam Institute in Jacksonville, Florida, and also with Dr. Carl Rossi at the California Proton Treatment Center in San Diego, CA. I had watched several YouTube videos of Dr. Rossi making informative presentations about his expertise with PBT. I became impressed by the proton beam technology.

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I asked the radiologist who had been more or less assigned to me at Mass General Brigham (MGB) why MGB offered PBT on its website, but when I asked about using it for PCa radiation procedures, I was told that MGB did not use PBT for PCa radiotherapy treatments. When I pushed for a reason why, the radiation oncologist (RO) told me that MGB didn’t use their PBT equipment for PCa care for “business reasons.” I had heard this from other men with whom I’d communicated on various patient portals about PBT in New England. This realization caused me to find a medical oncologist (MO) and a RO elsewhere. I moved to Dana Farber Cancer Institute (DFCI) literally down the street from the MGB facilities.

My PSA had continued to rise, so by the time it reached 0.21 in the spring of 2022, I was being cared for by Dr. Morgans at DFCI. When Dr. Morgans confirmed that my PSA had reached the magic biochemical recurrence (BCR) point of 0.21, and the PSMA PET CT scan revealed a 3 mm lesion on my left sacrum. We determined that my next treatment option should be radiation therapy. Frankly, being in Boston, where proton beam therapy (PBT) for prostate cancer (PCa) is not encouraged, I expected pushback from Dr. Morgans. This did not occur. By this time, I had chosen the Roberts Proton Beam Treatment Center at UPenn as where I wanted to go because I could avoid getting on an airplane. I could get to Philadelphia by Amtrak with less exposure to Covid infection. I had selected Dr. Neta Vapiwala as my radiation oncologist (RO) of choice, and I had contacted the UPenn facility myself. I explained this to Dr. Morgans, and I was delighted to learn that she and Dr. Vapiwala were friendly colleagues, and Dr. Morgans would happily make a referral to Dr. Vapiwala for me.

I went to UPenn in early August 2022 and completed the SRT using the PBT facilities at the Roberts Proton Beam Center by the first week in September 2022. I had no problems with the treatments other than some fatigue and lower back pain. I met with Dr. Vapiwala every week, and I mentioned the back pain. This surprised her, but she told me that some men experience some pain when their lesions become inflamed by the radiation. That pain usually passes quickly, but my discomfort was not subsiding.

Dr. Vapiwala ordered an MRI of my lower back. From the MRI she saw that the lesion on my sacrum was gone, but the MRI report revealed that I had five spinal compression fractures (CF). We determined that the back pain I was experiencing was probably caused by the CF. When I returned to my home, I was taking 50 mgs of Tramadol and 500 mgs of Tylenol three times a day to minimize the back pain.

I continually wondered if the pain in my back was caused by prostate cancer (PCa) growing in my spine and was not due to the orthopedic spinal compression fractures (CFs). I made an appointment to obtain a DEXA scan to check my bone mineral density (BMD) and determine the status of my bones. The scan results determined that I had a fairly severe case of osteoporosis. Not good news. I made an appointment with Dr. Jay Zampini, an orthopedic spinal specialist at the MGB Spinal Care Center in Boston. He ordered a CT x-ray and an MRI of my back during our first meeting. He examined my range of motion, what caused pain and when.

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After the MRI results came back from the MGB Spinal Center, Dr. Zampini and I had a tele-medicine conference. He explained that four of five spinal CF had healed, and he concluded that the pain I was experiencing was probably being caused by the fifth and as yet unhealed CF. We determined that I probably obtained the first CF during a diving accident while swimming in 1968. Thereafter, other CFs probably occurred as my osteoporosis advanced. The vertebrae had sort of pan-caked down like the upper floors at the World Trade Center after the lower floors that had been damaged by the fire could no longer support the weight of the above floors. This made sense to me. I had had several bouts of lower back pain over the years, but I had treated these events by seeing chiropractors and not having my spinal pain orthopedically evaluated.

Dr. Zampini explained that at MGB, he no longer recommends the use of spinal fusion surgery to immobilize the compressed vertebrae unless there has been nerve damage, which the MRI of my spine had not identified. He told me to begin physical therapy (PT) and to consider seeing an endocrinologist about which medicine to use to improve my BMD. I asked Dr. Morgans to refer me to an endocrinologist, and I scheduled an appointment at DFCI. Several of my Cancer Patient Lab colleagues and other patient portal colleagues had been counseling me to see my dentist and get all of my dental work up to date to avoid future osteonecrosis problems.

I began PT, and started using Dr. Lawrence Fishman’s exercises from his book, *Yoga for Osteoporosis.* I have been walking for about an hour everyday using walking poles for stability. I am following Dr. Doug McGuff’s exercise protocol as outlined in his book *Body By Science* for weekly weight training exercises at our local Northampton Senior Center. I can feel that I am building some strength and the lower back pain is diminishing. During this time my PSA has continued to rise from a low point following my stereotactic radiotherapy (SRT) at UPenn.

Our Cancer Patient Lab colleague, Dr. Allen Morris, a pathologist and a fellow PCa warrior has suggested that I may be classified as an Oligometastatic Patient, in my case with one sacral bone metastasis, who received not only prostate bed salvage RT but also Metastasis Directed RadioTherapy (MDT) to the sacral metastasis. He explained that although my present PSA has reached 0.21 once again, this does not mean that I have reached biochemical recurrence (BCR) for a second time. It appears that my PCa progression following the PBT at UPenn may have reached a PSA nadir of 0.14 for the period of time 1/22 thru 7/23.

My PSA has now risen to 0.21. This is a 0.07 increase over a possible PSA nadir of 0.14 following the SRT treatments. Dr. Morris has suggested that the PBT SRT may have continued to kill the PCa cells within the targeted treatment areas, and the radiation may be continuing to kill cancer cells for a period of time as long as a year or more. Dr. Morris believes that PSA doubling time is a meaningful determinant, but not with my current low values. Furthermore, the current values are probably confounded by ongoing proton radiotherapy death. And that only continuing monitoring and future values will determine if PSA doubling time can even be evaluated. To me, this explanation makes sense. I have never considered this arithmetic calculation of future determining future BCR events.

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[AM editorial: The BCR we are talking about would be status post (s/p) metastasis directed radiotherapy to a single small, presumably 3 mm, sacral bone metastasis. This type of BCR has never been defined.

To repeat, there really is no established concept of this 3rd type of BCR.
In fact, the current and long standing paradigm, is if you declare yourself as metastatic, which Jeff has by virtue of his sacral bone metastasis;
Jeff is now labeled as having metastatic prostate cancer period, going forward in his journey.
By the conventional paradigm, right now Jeff is metastatic hormone-sensitive prostate cancer (mHSPC) despite having been rendered No evidence of disease (NED) by Proton RT (MDT).
For example, Jeff can never be labeled non-metastatic Castrate resistant PC (nmCRPC).
So, if Jeff is rendered no evidence of disease (NED) by metastasis directed therapy (MDT), which he has and
Jeff is put on hormone therapy including if he decides to N of 1 experiment on himself with BAT, when Jeff no longer responds to the low (ADT) END of BAT, as evidenced by rising PSA despite castrate testosterone levels, even if Jeff’s radiology studies continue to be negative, Jeff will not be considered nmCRPC, even though Jeff has no metastatic disease visible on radiology scans; rather Jeff will be considered mCRPC.
In other words, Jeff will not be considered to have reverted to a better stage, just as if lower tumor burden, lower tumor mutational burden, lower CTCs etc; will not be a new lower status/stage; but rather one would just be considered to have responded as expected to the low end of (ADT) therapy.
History lesson: In the 90s, there was a belief that neoadjuvant Lupron could cure prostate cancer. Lupron alone was that good at rendering a prostate NED; neoadjuvantly.

So let us review the concepts of 1st, 2nd, and 3rd BCR:
1. 1st BCR refers to rising PSA after primary curative treatment: innumerable papers
2. 2nd BCR refers to rising PSA after (curative attempt) salvage RT usually to the prostate bed sometimes with extended pelvic LN coverage: well studied
3. 3rd BCR after metastasis-directed therapy: virtually not studied at all, except for a few phase 2 studies including ORIOLE, SABR-COMET, and STOMP and is usually termed PSA progression

I believe the concept of a BCR s/p MDT to a bone metastasis will bring blank stares from 98% of the urologic community.
Because it is a supersaturated solution, many, including myself, have spontaneously conjured up the term BCR, rising PSA, after metastasis-directed Radiation therapy for this 3rd possible instance.

The Phoenix definition of BCR status post radiotherapy after either initial curative intent RT or after initial salvage prostate bed +/- pelvic field is PSA nadir + 2.0 ng/dl.
Using the Phoenix definition, Jeff would need a PSA of 0.14 (assuming this is his nadir) + 2.0 = 2.14 ng/dl. This definition is impractical for Jeff vis a vis the conventional wisdom of curative intent radiotherapy being most effective when PSA is <0.5 ng/dl.
Note: In the new paradigm of OMPC, each new instance of a +PSMA PET/CT scan result with less than or equal e.g. 3 metastases would still qualify one for another round of MDT as an

“oligo progressive” patient. Presumably, allowing for another round of “kicking the can down the road”.

So what would BCR for a 3 mm sacral metastasis be? Answer for Jeff: PSA nadir 0.14 + what large number? Probably < 2 ng/dl, but nobody knows; not even Dr.Sartor.]

[AM references a youtube video on Oligometastatic Cancer, primarily aimed at Prostate Cancer, with Drs. Feng and Hong of UCSF.

Important note: This video uses the term "Biochemical Recurrence" (BCR) and the word "Cure" in reference to Oligometastatic Prostate Cancer (OPMC).

This video actually uses the term "Biochemical recurrence" in an outcome/endpoint graph vs. Time for efficacy of Metastasis Directed Therapy from the STOMP study. The graph is listed at time 36:56. Interestingly at about 4 years out, the BCR free survival is around 25%, in keeping/supporting Dr. Rossi's claim of 30% cure with MDT. This assumes BCR free survival (inversely related to Time to BCR) at 4 years is equivalent to "cure".

Dr. Feng, at 41:50, in reference to a PC patient, who has a single pubic ramus (pelvic) bone metastasis who Dr. Feng treated with Metastasis Directed Therapy (MDT), SBRT(Stereotactic Body Radiotherapy), used the word "cure".
Sounds similar to your case Jeff: What do you think?
From the above, not only are Hong and Feng using the term, but the authors of the Stomp study used the term: Biochemical Recurrence.

Can Radiotherapy Cure Stage IV Cancer? The Future of Oligometastatic Cancer

Reference for the ORIOLE trial:
Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer

Very Important note: In the ORIOLE study PSA progression (I believe a synonym for Biochemical Recurrence) is defined as a PSA of >2ng/dl.
Note: PSA >2ng/dl is close to the Phoenix definition of BCR post primary or salvage RT which is PSA nadir + 2ng/dl.

Concerning you Jeff, you are far from 2ng/dl. However, as I stated below, I believe your magic number is <0.5 ng/dl, per getting a PSMA PET/CT scan.
Jeff. Keep us posted as to your monthly PSA levels. We will help you calculate a PSA Doubling Time.
The PSA doubling time is your single best metric determining your current prognosis.
The results of your PSMA PET/CT scan will refine the prognosis.

Per References for STOMP, ORIOLE, and SABR-COMET:
Here is a 2022 look at both STOMP and ORIOLE combined:
Long-Term Outcomes and Genetic Predictors of Response to Metastasis-Directed Therapy Versus Observation in Oligometastatic Prostate Cancer: Analysis of STOMP and ORIOLE Trials | Journal of Clinical Oncology]

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At this point in time, I have met with the DFCI endocrinologist by telemed conference, and he has ordered a selection of blood tests to determine if the supplements that I have been taking are appropriate and if my present hormonal levels are within normally acceptable limits. He has suggested several BMD medications to consider using following the completion of my dental repairs. The dental work should be completed by the end of September. I have a panel of blood tests scheduled for mid-September when I will meet with Dr. Morgans again to evaluate my PSA level and consider future treatment options. We have discussed getting a PSMA PET CT scan in October given that I will be close to eighteen months since I had my last PSMA PET CT scan.

We discussed the eventual possibility of hormone therapy for me. When I mentioned using tE2 as a form of androgen deprivation therapy (ADT), she was noticeably resistant, but she told me that she would not reject me as a continuing patient, but she could not deviate from the standard of care directed by her profession and the institution where she is employed. We chatted about the Cancer Patient Lab and the men doing bipolar androgen therapy (BAT) who are members of the Cancer Patient Lab. I think she is interested in discussing what we discover going forward.

If I find that I need additional radiation to treat lesions that may be detected from a PSMA PET CT scan in the fall, I intend to return to UPenn to be treated by Dr. Vapiwala. At that time, I discussed being treated prophylactically with PBT for gynecomastia (a condition of overdevelopment or enlargement of the breast tissue in men). I have experienced gynecomastia in my left breast. I had a mammogram, and the findings were negative. If I eventually use hormone therapy and some form of tE2, it makes sense to treat my breast areas before I begin hormone therapy.

Brian McCloskey 17:11
There's a lot going on with your history. I'm wondering if you could help to guide the audience just a little bit in terms of the key decisions that you have to make in priority order? Like what do you need help with the most right now?

Jeffrey Dwyer 17:41
I think my next decision will be picking one of the three or four bone mineral density (BMD) meds. I've been encouraged by Paul Van Camp, and by Richard Wassersug to select a BMD med and begin treatments. I see my cardiologist in August, and I want to discuss his experience with the various BMD medications before I make a final selection. I think that one of the tests that should be standard of care (SOC) when anyone begins the PCa journey should be a DEXA scan as part of a patient’s analysis. If I had known that I had osteoporosis, which has not been in my family history, I would have begun BMD treatment a long time before I might now need to have hormone therapy.

Brian McCloskey 19:02

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The good news is that we've got a couple of people that might be able to help you with respect to understanding the pros and cons of some of the bone density or bone strengthening drugs. I hate to put them on the spot, but I'm going to do that. They can differ if they don't if they don't want to answer, but Robert Gurmankin, who's a dentist, and of course we have Rick Stanton on the line as well, who was deeply involved in the development of Xgeva and Prolia. So any thoughts guys?

Robert Gurmankin 19:56
In terms of osteonecrosis (obstruction of blood flow) to the jaw, his chances of getting it are certainly higher with these drugs, but a compression fracture, or fractured hip, that's a whole different ball game compared to getting osteonecrosis to the jaw (ONJ). ONJ is nothing compared to that. In most cases, though, not all, it is reasonably mild. So I wouldn't let that stop you. Just make sure any dental work that you need done is taken care of. If you have anything that has to be done, get it done; anything that's iffy, get it done. What makes the most likelihood of getting ONJ: any kind of dental treatment that is invasive, extractions, gum therapy, anything that's going to need remodeling of the bone, and can have infiltration of bacteria into the bone. You want to just make sure that you have really good oral hygiene so that you don't get future problems. I think I sent an email about prescription fluoride treatment.

Jeffrey Dwyer 22:03
I got that prescription yesterday. Thank you for suggesting it in the email you sent me.

Robert Gurmankin 22:07
Yeah, and pristine oral hygiene.

Rick Davis 23:56
You should look into getting radiation to your chest before you start. I've talked about this for years with docs including cardiologists. Most of them feel that there's little or no risk. Given the amount of radiation it usually is two or three sessions. For some guys. It really works well. But not for everybody. But it is the best solution if it works to avoid gynecomastia.

I don't have enough knowledge about, but I'm intrigued that since cardiac issues are involved, is whether a monotherapy ARSI (androgen receptor signaling inhibitor) might be a good option. In other words, you still will have testosterone running around in your system, but you're blocking it at the receptor level. In theory, it should have just as many side effects, but it just doesn't seem to because we know enough guys who have been on monotherapy apalutamide and darolutamide, actually not Enzalutamide, and on monotherapy Abiraterone, which is a little different, which I don't think would work as well, but I would look into it. I would explore with Dr. Alicia Morgans, whether that might work, and I also think that I mentioned to you that Dr. Vivek Narayan is a really good guy at UPenn. He works closely with Dr. Vapiwala. He has a particular interest in cardio health. He is scheduled to do a research project with AnCan at some point when they get their act together. A consult with Dr. Narayan will be very helpful in terms of monotherapy.

“Treating My Osteoporosis and My Prostate Cancer” (Jeff Dwyer) [#65]

Jeffrey Dwyer 26:38
Since I have gynecomastia in my left breast. Dr. Morgans had me get a mammogram, which turned out to be negative for breast cancer but confirmed gynecomastia. I contacted Dr. Vapiwala about pretreatment radiation. And she said, “ Yes, come on down. We do it all the time.” Thanks, Rick, I appreciate your suggestion.

Rick Davis 27:31
If you're going down there, set up a time to see Dr. Vivek Narayan as well.

Jeffrey Dwyer 27:38
I'll make it a point to write him a letter and tell him who I am and ask him if I can consult with him.

Rick Davis 28:11
You can tell him we sent you, You can tell him we recommended you because AnCan has a nice relationship with him.

Rick Stanton 28:27
For Robert Gurmankin: Is there any reason why not use Xgeva?
(Denosumab can treat osteoporosis and bone problems in patients who have cancer.)
I'm taking Xgeva now.

Robert Gurmankin 28:47
I'm on Xgeva as well. They all have similar risks as far as osteonecrosis. The only difference is, you gotta be careful once you stop, there can be a rebound effect with Xgeva. I've had no side effects. I don't know about you. Some people get it monthly, but they seem to be going more quarterly. So that should decrease the risk of ONJ. But any of these drugs will give you like a 2% or 3% chance and again, 80% of the people get it after having some kind of trauma, even if it's controlled trauma to the jaws.

Rick Stanton 29:48
So maybe it would help, Jeff.

Robert Gurmankin 29:52
If you go on the estrogens that may help keep the osteoporosis from getting worse, but it's not going to improve it, I wouldn't think. Xgeva or any of the bisphosphonates can help rebuild some of the bone. And again, the chances of osteonecrosis are pretty low.

Rick Davis 30:27
Can I add some personal experience on osteoporosis and bone strengthening that may be helpful? When I was diagnosed in 2007, and being placed on long term hormone therapy, my doctor ordered a DEXA scan, which is standard of care, although a lot of doctors don't do it. And it turned out I was osteoporotic, in my spine, which was pretty weird to me, because I was running about 3000 miles a year at that point. And I got it because there wasn't any clear

metastasis. In my case, it was micro metastasis. I got three infusions of Zometa over two years, one at the beginning, one in the middle, and one at the end of the two years. And I also changed my exercise habits, and specifically work to put stress on my spine in my exercise. And at the end of the three years, my bone density in my spine had gone from minus 2.5 to 0.9. Now it's gone back again. So I’m now osteopenic again, but they can be done.

David Plunkett 32:05
Some personal anecdotes. When I was first diagnosed, I was given a DEXA scan early on and discovered that I was osteopenic. So I was given an infusion of Zometa. And I had a reaction to that. That afternoon and night, I had a fever, it topped out at 100 Fahrenheit. So just below the threshold where they had told me I needed to go to the ER. It only lasted about 12 hours and never came back. But that was enough of a reaction that six months later, instead of the next infusion of Zometa, they switched me to a different medication, Prolia, which is denosumab. Prolia didn't give me any reactions at all. It may have slowed the loss of bone density, but it did not stop it. So for the next cycle, they changed me to Xgeva, which is the same stuff, only a stronger dose. That seems to have been more effective for me. And again, no side effects. I don't know why the doctor preferred to start with Zometa, or whether that's just standard practice. But apparently the reaction I had was pretty unusual. If I hadn't had that reaction, they probably would have continued with it. But it's worked out well for me ever since. I'm still on Xgeva every quarter.

Russ Hollyer 33:34
I did transdermal estrogen therapy by myself. My medical oncologist (MO) was monitoring me. It's really not very hard to do. 0.3-0.4 milligrams a day estrogen Climara patches worked very well for me and took my testosterone to zero in about five weeks. I had a DEXA scan about a decade ago. I had osteopenia. Estrogen-ADT appeared to decrease the rate of decline of my bone decay. When I went to BAT my bone density increased by 4.0 to 5.2%. Depending on what scans I look at, what measurements I look at, I've had three DEXA scans. My bone mass also increased over 4%.
ARPI monotherapy has been studied. So it's not only anecdotal. We see reduced bone density decay.
There are also anabolic steroids such as nandrolone. It's an FDA approved steroid. Oxandrolone is another one. Nandrolone has been shown to increase bone density. So that's another possibility to look into. It's not very androgenic. So I see you having at least four possibilities to look into: ARPI monotherapy, BAT, transdermal estrogen therapy, and nandrolone. In addition, I would jump on board with Xgeva, or something to address bone loss immediately.

Russ Hollyer 36:49
Concerning the transdermal estrogen therapy, It has been shown to be non-inferior to Lupron. If you look at the PATCH trial results, bone loss is decreased and cardiac events are decreased too.

Jeffrey Dwyer 37:25

I read that in the STAMPEDE trials that was done in the UK that tE2 was superior to other ADT drugs as far as cardiac events were concerned.

Russ Hollyer 37:40
They will say they're equivalent because I don't believe that reached statistical significance. So they have to say, “Yeah, we're equivalent.” But if you look at the results, you have fewer cardiac events and less bone loss. Another thing, if you start the transdermal estrogen therapy, make sure you get a patch that only has estradiol. For example the Climara Pro has estradiol and progestin.

Brad Power 38:58
It would be useful for you to share with the group here the conversation you have with Allen Morris about Gleason score as a measure of the aggressiveness of your cancer and then what constitutes recurrence. And then how do you measure doubling time? You alluded to it, but I learned a lot just from that conversation. It was really interesting in your case, because the aggressiveness of the cancer influences the aggressiveness of your treatment. And just as Bob Gurmankin was saying that maybe there's not that bad of side effects, you need to know how aggressive you should be, and you're going to gear that a little bit on a prediction about the aggressiveness of your cancer. And he was much more nuanced in that argumentation.

Jeff Dwyer
When I got back to Massachusetts, I got a PSA test at my local affiliated hospital to MGB. And it was higher. I just assumed the two professionals were talking. But it turns out they weren't. And so I watched my PSA go high, then down, and then climb up to 0.21. And Allen Morris explained to me that that's an arbitrary number. He looked at my PSA chart that I’ve showed you guys. And he said, I think your nadir PSA is 0.14, and you've now been steady there for six months. And now it's up to 0.21. So it's risen, you know, 50%. But it has not risen up to another biochemical recurrence, you have not reached that yet. Which was a very nice thing to hear. He said, Really, if you look at it and do the rough arithmetic, you won't reach biochemical returns until it's at least 0.28 or greater. So, which could be in October, I'll be a year from SRT. And he explained to me that my radiation therapy is still killing my prostate cancer cells in the targeted area, which no one had explained to me, nobody, not Dr. Vapiwala, nor Dr. Morgans. Maybe they just assumed that I knew it. But I did not. So I came away from the discussion with Allen Morris feeling encouraged that my PSA may just stay at a certain level and may not rapidly rise. It might rise tomorrow, but right at this point in time, it doesn't seem to be.

Brad Power 43:55
So let me just summarize this. Where I think this leaves us is that you thought you had a recurrence. And if you have a recurrence, then you need to go get on some prostate cancer drugs like androgen deprivation therapy. But he challenges that very premise, and says, "I'm not sure if you've had a recurrence yet. You could still be cruising along sideways." And you don't need to get any prostate cancer treatment at this moment. And so you can worry about your other comorbidities, worry about your bones, or worry about your heart, and you're saying you

maybe don't need to worry as much about your prostate. So this is pretty important in guiding your next steps, if I'm understanding correctly.

Jeffrey Dwyer 44:36
Yes, and I had the same guidance from one of my friends who is overseeing her husband’s prostate cancer treatment, and she felt the same way. She said, “I just realized you haven't recovered from your SRT yet.” And of course, I don't listen to anybody, and I just keep reading, but I keep looking and wondering where I am. It will be interesting to see what happens with the next PSA. Allen's final email to me last night was at 11:00 PM – he's been terrific – He said, “Get your PSA monthly, then a PSMA PET if you can, because that's going to best tell you where you are.” And Dr. Morgans said that, at least at Dana Farber, they will get some pushback from Medicare if the PSMA PET is more often than one time within a year, but over a year, they don't get any pushback for getting PSMA PET, so I'll probably get it done sometime in the fall.

Rick Stanton 45:48
I echo Rick Davis's comment, I'm getting PSMA PET scans quarterly. Medicare's covering them. Rick really hit the nail on the head there. And then the second thing is, at least when PSMA scans were started, I believe it's only a few years old.

Jeffrey Dwyer 46:15

Rick Stanton 46:20
I was told at UCLA that if you have a PSA under 0.6, there's a pretty good chance they're not going to detect anything. So just a couple of things that I think are true.

Jeffrey Dwyer 46:40
What was interesting was when I went out to the Veterans Administration in LA in the summer of 2021 for that trial, Dr. Bahrani, thé RO in charge said, “I've seen men with mets with PSAs well under 0.2”, because I'd heard that with 0.2, not to waste my time. In fact, Dr. Rossi said, “Don't waste your time.” But of course, like I said before, I don't listen to anybody. So I asked Dr. Bahrani, and he said, “I've seen our vets here with mets and with their PSA reading under 0.2. So if you want to, come out.” It was just the cost of an airline ticket and the hotel. So that's what I did. And, and he was right. I mean, I didn't have anything except the dye in my urethra, but at least I now had a PSMA PET baseline. So when Dr. Morgans ordered the next one when I did reach 0.21, she had something to compare it to. So I've had two PSMA PETs now, but it'll be interesting to see if anything shows up on the next one.

Russ Hollyer 48:16
I agree with getting a PSMA PET scan. Remember that PSA is not cancer. My MO (medical oncologist) would likely disagree with doing nothing based on your Gleason score and potential aggressive behavior. I'd consider talking to some MOs to get their opinions and their advice.

Jeffrey Dwyer 49:57

That's the path I'm on now. So we'll see.

Russ Hollyer 50:03
I wanted to mention that clinical trials show that around 25% of guys with your PSA have at least one met that show up on PSMA PET scans. If you get to a PSA level of about one it climbs to something like 90%.

Rick Davis 50:33
As a couple of guys in this session will testify, we spoke about two of these issues yesterday in the AnCan meeting. Here is the link: https://youtu.be/0zkmtr__CXI

On this PSA level when you do PSMA scans, in the literature – I think it was the VISION trial – essentially there's less than a 40% chance of seeing anything on the scan if your PSA is less than 0.2. It doesn't mean you won't see it, but your chances are reduced. If your PSA is above 0.6, I think it's 0.6, 0.5, actually, it's around an 80% chance that you'll see something. So really what you're doing is you're rolling the dice. The thing to note, and a lot of people don't get this, is that this really is designed for people who don't see any metastasis. Like say, Jeff, and they're trying to figure out where their metastasis is if you know you have metastasis, and you want to see how it's changed. You could be on ADT and have a PSA of zero, because the metastasis expresses PSMA. In fact, the more advanced the metastasis is, the more PSMA it shows, and so you can be sitting there, you can do a PSMA scan with zero, and it's going to show where the mets are. We had a guy yesterday talking about the fact that they just saw a lesion on his bladder wall even though he's on ADT, and his PSA is insignificant. And we said to him, you have a couple of options you can do. You can do a Cystoscopy, and you can get a biopsy. But you could also do a PSMA scan first, and if it shows up positive, you don't need the biopsy. If it doesn't show up positive then do the biopsy. And then somebody said well, I just go get a biopsy. Fine. But in the interest of doing no harm, the least intrusive, the PSMA scan, which would show it if it was expressing PSMA. So you have to bear that in mind when you're thinking about the PSA levels.

Brian McCloskey 53:41
One of the things we haven't talked about is any genomics that you have. And given that your PSA is low, you may not have had any liquid biopsies. But just curious if anyone's looked at your genomic profile and indicated that you have markers that would indicate you have aggressive cancer.

Jeffrey Dwyer 54:06
I did have it done. Dr. Morgans ordered it, and I've gotten the results. And it came back with I think 28 genetic markers and none of them showed that I had anything pointing towards prostate cancer. I asked Dr. Morgans about getting liquid biopsies, and she said because your genetic profiles showed none in your DNA, you probably won't show any in a liquid biopsy either at this time, but she said we can do it next time if you want to. She doubts they'll show anything because it's doubtful there is anything circulating right now that they can measure.

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Brian McCloskey 55:01
A challenge right now with your PSA being so low.

Russ Hollyer 55:09
I would tell your MO that, while it's doubtful that you have genetic mutations you want a somatic blood test anyway.

Brian McCloskey 56:02
Did they find any mutations?

Jeff Dwyer 56:07
They did not find any mutations.

Russ Hollyer
That's not the only information you get. You might get some analog measurements. For example I received info on CTCs (circulating tumor cells) used to calculate a tumor mutational burden. Because I had a baseline test and quarterly snapshots, I can see that my tumor mutational burden has gone down since I started BAT, and now can’t be quantified because I don’t have enough CTCs to measure. It's just a simple blood test. When I have mine done I lump it in with PSA, testosterone, CBC, and CMP.

Jeffrey Dwyer 57:18
Yeah, they've got me scheduled for it. I failed to mention that I did see the endocrinologist and we went through all of the supplements I was taking, and he ordered a bunch of blood tests: magnesium, calcium, all that. I have to get those blood test soon. I can probably get in touch with Dr. Morgans and ask her to add that liquid biopsy now because I haven't gone and gotten those blood tests yet, but the orders are in. So I'll ask her to add the tests. Thank you.