“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]

Russ Hollyer and Brad Power
May 17, 2023

“If we continue to do the same things, we will get the same results.” – Russ Hollyer

“If BAT can be used to sensitive Xtandi/darolutamide ad infinitum, prostate cancer becomes a treatable condition like diabetes.” – Russ Hollyer

Meeting Summary

Advanced prostate cancer patients who are failing the standard hormone (androgen) deprivation therapy (“castrate resistant”) are interested in finding new options. Bipolar Androgen Therapy (BAT, where high doses of testosterone are alternated with androgen deprivation therapy) potentially offers a number of unique benefits. It aims to:

- Control disease progression (as measured by prostate specific antigen/PSA and PSMA PET scans) for a sustained period
- Restore sensitivity to androgen therapies (e.g., Xtandi)
- Improve quality of life and also improve other health markers.

The clinical evidence supporting BAT is small-scale, and only for a portion of patients. It isn’t included early in the standard of care. It doesn’t have any pharmaceutical companies promoting its use since it depends on easily available, relatively inexpensive testosterone. Yet many advanced prostate cancer patients in our community who don’t have time to wait are trying BAT or seriously considering it.

We have had three previous discussions of adaptive therapy (where treatments are tuned to a patient's biomarkers, e.g., PSA level) and BAT.

- Bob Gatenby, MD, from Moffitt Cancer Center, introduced adaptive therapy -- using evolutionary and game theory to inform cancer treatment strategy.
- Advanced prostate cancer patient Bryce Olson shared the story of his exceptional response to BAT and then Bob Gatenby commented on Bryce’s experience and strategy.
- Emmanuel Antonarakis, MD, spoke about using BAT for advanced prostate cancer.

What Does It Take to Choose BAT?

- First, most patients and oncologists are not aware of or considering BAT as an option. Pharma won’t fund trials for this treatment because they would not return a profit.
- Second, the patient has to be brave enough – we have been taught for years that taking testosterone can be like throwing gasoline on the fire, feeding cancer growth.
- Third, the patient must find a doctor who is willing to support it or be willing to self-administer (typically with monitoring by an MO).

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About Russ Hollyer

Super patient Russ Hollyer is uniquely qualified to share a patient's view on BAT. He has been self-administering BAT and has written a book about his experience. Russ is a "citizen scientist", applying his expertise in science (reviewing research papers, running experiments, accessing drugs, testing, monitoring progress) to his own treatment.

Russ has advanced prostate cancer, Gleason 9, and was diagnosed in 2018. He had a radical prostatectomy (RP) later that year, estrogen/Zytiga androgen deprivation therapy (ADT) in 2019, followed by high testosterone, followed by do it yourself (DIY) BAT. Each BAT treatment involves the self-administration of hormonal ablation or hormonal extremes.

During his work career, Russ worked as an electrical engineer for a medical company, an aerospace engineer for the government and contractors, and as a hedge fund manager. Most of his work was in the medical technology area and involved data gathering, quality screen design, computer programming, and test screening. Because of this he became very data-driven. He determined from experience that theories and hypotheticals are very frequently proven to be incorrect.

Discussion Agenda

1. Description of BAT: how it works
2. Russ's experience: PSA, cancer progression, RBC, WBC, liver markers, bone density, libido, and fatigue during that time
3. How to improve BAT

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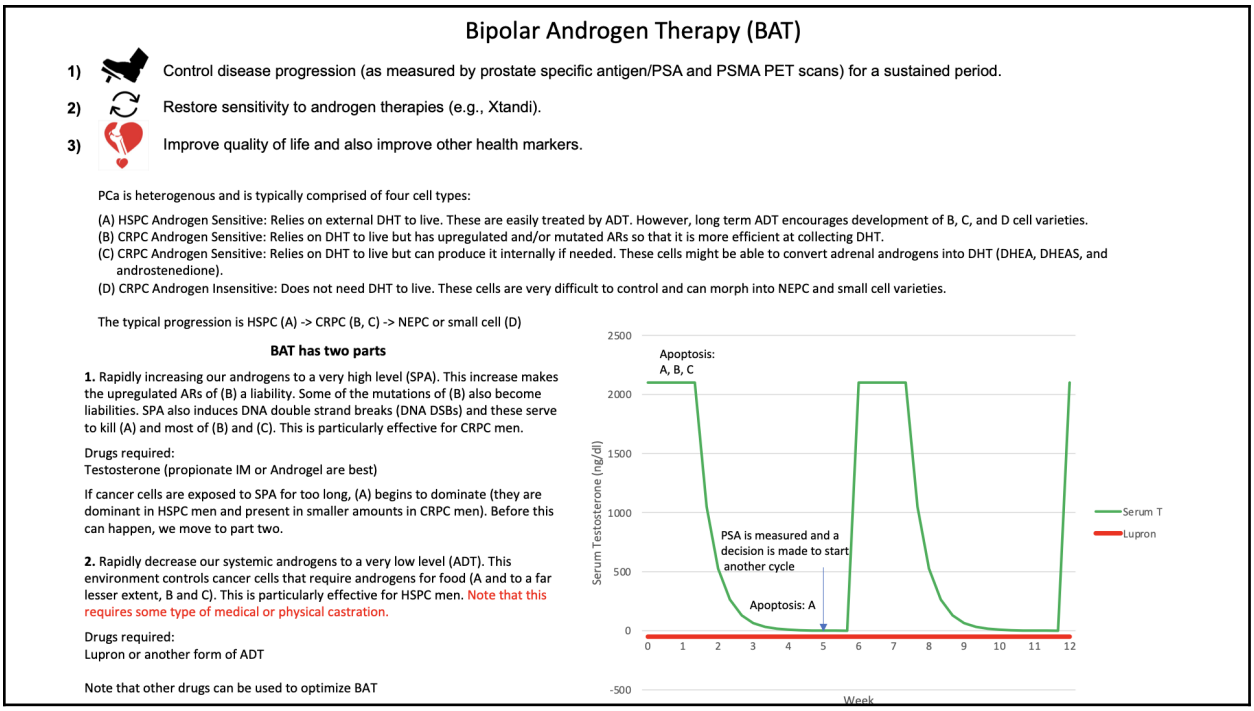

1. ***Description of BAT:*** *How does depriving then flooding cancer cells with hormones (androgen) control the prostate cancer population?*

Cancer cells in a prostate cancer (prostate cancer) patient’s tumor are heterogenous and can be categorized into four distinct cell types:

A. *Hormone (androgen) sensitive*: These prostate cancer cells rely on an external form of testosterone (dihydrotestosterone - DHT) to live. These cells are easily treated by androgen deprivation therapy (ADT).
B. *Androgen sensitive and unresponsive to androgen deprivation therapy (ADT)*: These cells rely on DHT to live, but have upregulated and/or mutated androgen receptors (ARs), so that these cells may be more efficient at collecting DHT, and don’t respond to androgen deprivation therapy (ADT).
C. *Androgen sensitive and unresponsive to ADT and produce testosterone internally*: These cells rely on DHT to live but they have mutated to be able to produce DHT internally if needed. They might be able to convert adrenal androgens (Dehydroepiandrosterone - DHEA, dehydroepiandrosterone sulfate - DHEAS, androstenedione delta 4) into DHT.
D. *Androgen insensitive*: These cells do not need DHT to survive and grow. They are very difficult to control and can morph into neuroendocrine prostate cancer (NEPC) and small cell varieties.

When you use androgen deprivation therapy (ADT), your goal is to drive testosterone down as low as possible and starve the prostate cancer cells of their growth fuel. This process deprives androgen sensitive cells (type A) of that “fuel”. Initially this appears to be successful. Usually during the early stages of prostate cancer development, most cancer cells are androgen

sensitive (type A), and most of them die when androgens are withheld. This is hormone sensitive prostate cancer (HSPC). However, as type A cells are killed off and decrease in number, type B and C cells mutate and begin to grow, and type D cells will also appear.

Eventually, the patient’s prostate cancer is composed of cells that can live in low androgen conditions (called Castrate Resistant Prostate Cancer - CRPC). The change from HSPC to CRPC typically takes 1-4 years. When prostate cancer is castrate resistant or beyond, it becomes much harder to control.

If you have CRPC, you can use hormones to shift the population of your prostate cancer back into type A prostate cancer cells. Clinical trials are showing us that by using bipolar androgen therapy (BAT), most patients can restore their sensitivity to androgen receptor blockers/androgen receptor signaling inhibitors (ARBs/ARSIs). The desire is to cause prostate cancer to become a chronic disease and not a killing disease.

BAT has two parts:

1. Rapidly increase your androgen to a very high level (Supraphysiological - SPA). This increase makes the upregulated ARs of type B cells a liability. Some of the mutations of type B cells also become liabilities. SPA also induces cellular DNA double strand breaks (DNA DSBs) and these cellular breaks serve to kill type A, B, and C prostate cancer cells. If cancer cells are exposed to SPA for too long, (A) begins to dominate (they are dominant in HSPC men and present in smaller amounts in CRPC men). Before this can happen, with BAT, the patient moves to part two of the BAT process.
2. We rapidly decrease the patient’s systemic androgens to a very low level. This changed environment controls cancer cells that require androgens for food (type A cells, and to a far lesser extent, type B and C cells). This is particularly effective for HSPC men. Note that this requires some type of medical or physical castration. ADT drugs are that chemical castration.

Supraphysiological levels of androgen effectively inhibit growth of some CRPC cells but also inhibit growth of some HSPC cells. If a true ADT castration level is obtained in the second phase, inhibition is far greater in HSPC cells than in CRPC cells.

The HSPC -> CRPC transition is not binary. We do not know where the threshold of supraphysiological repression lies. If you can prevent HSPC -> CRPC progression, prostate cancer might become a chronic disease. Almost a dozen trials (RCT) have been performed on CRPC men with results ranging from decent to very good. One trial was performed on HSPC men with good results. Note that this trial used 3 standard 1-month testosterone cypionate BAT cycles followed by 3 months of the ADT cycle. This trial was called “Batman.”

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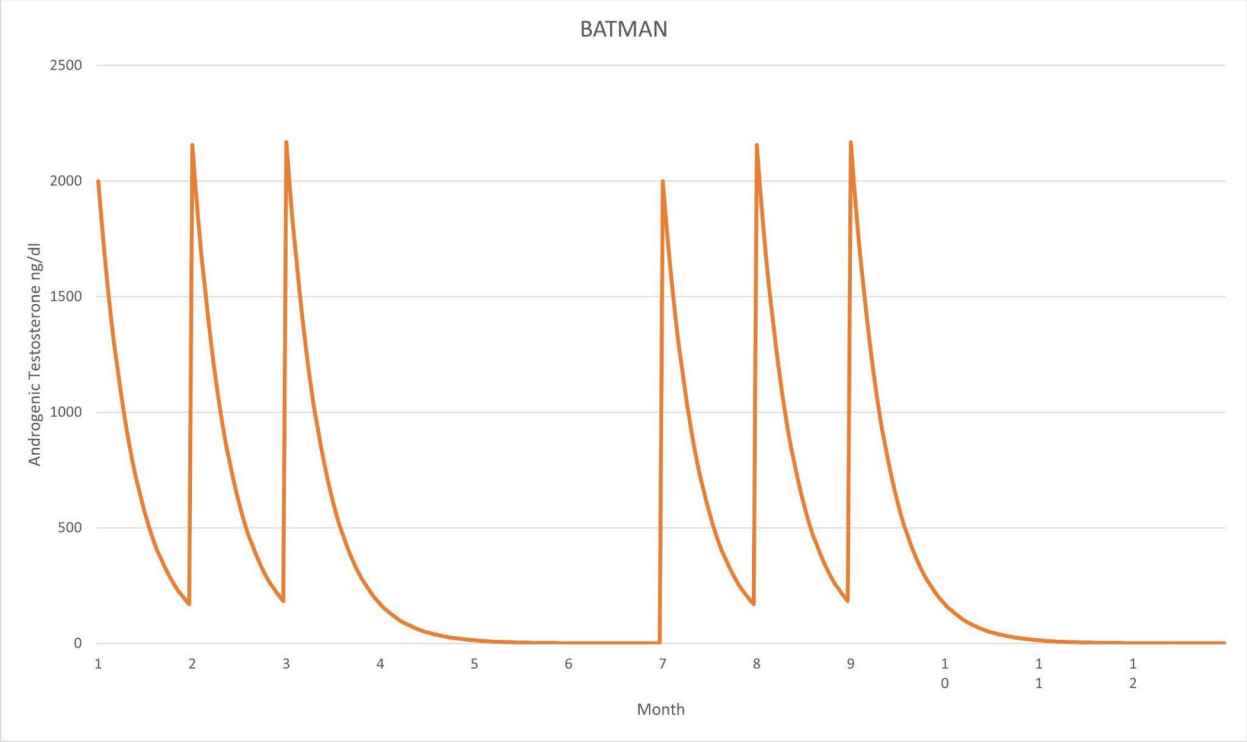

The longer ADT can be delayed, the better.

The quality of life (QOL) benefits of BAT argues for its use even if it isn’t as effective as ADT alone.

2. What has been Russ’s experience?

Russ uses Lupron for his ADT cycle of BAT continuously in order to remove endogenous testosterone produced by the body.
He uses testosterone propionate to achieve high levels of androgens.
A true ADT level will not be attained by using the standard 400 mg testosterone cypionate injections during the 4-week cycles. Russ uses testosterone propionate instead, and by so doing, he attains a true desired ADT level.

Russ monitors prostate specific antigen (PSA) with blood tests and uses the level of his PSA results to guide the termination of the ADT phase of BAT to begin a new supraphysiological androgen (SPA) phase. Using PSA is a crude marker of prostate cancer progression. Ideally, scans and genetic tests should be performed to monitor therapeutic progression of prostate cancer and the success of BAT. Sometimes PSA will increase but conversely radiological scans will show no growth nor regression. Along those lines, sometimes conversely increased bone met activity appears to occur for about 2-3 months before reductions begin to be seen.

PSA might rise for a couple of months following the start of BAT. This does not necessarily mean that BAT is failing. Sometimes it requires time for BAT to begin working. Sometimes

scans will be at odds with PSA blood testing. One should always rely upon the scans. What can be confusing is that sometimes a PSA will increase for a couple of months, and scans will simultaneously deteriorate. When this conflict occurs, then, it becomes a judgment call whether to continue the BAT procedure or terminate it.

If bone pain occurs, it is probably caused from inflammatory factors and not from growth of the cancer. Pain can be tested by administering 300 mg of transdermal Androgel. If you have pain, Androgel will wash out in a few days.

If muscle pain occurs, this can be reduced by taking NSAID meds such as Ibuprofen or Aleve. One might need to use high doses of these meds because both Ibuprofen (Motrin) have a very short half-life. Thus, the med dosing might need to be done every 3 or 4 hours. Aleve has a much longer half-life, and one might find that a single or second dose each day will help,to reduce the muscle pain.

Russ’s PSA when he began BAT was 0.17 ng/dl. After a little more than a year, his PSA had dropped to 0.02.

Russ had osteopenia for years, and it was becoming worse as time progressed. Transitioning into Osteoporosis appeared likely. During his first year of BAT, his bone mineral density (BMD) increased 5.20% as determined by a DEXA scan. Half a year later, he verified using a DEXA-FIT scan results had increased by 4.0%.

His sexual libido did not exist during ADT. But his sexual libido returned during SPA and has continued during BAT, however not as “actively” as he was during the SPA phase of BAT.

His muscle loss was reversed.

He has noticed that he has more energy during the SPA phase of BAT.

3. How can BAT be enhanced?

Statements have been made that BAT was used to treat CRPC men in clinical trials because guidelines to obtaining FDA standard of care (SOC) approval would be easier to achieve. But, other opinions acknowledge that BAT might be effective for HSPC patients too. However, the primary focus presently is for the treatment of CRPC patients. The BATMAN clinical trial was performed on HSPC men, and had very good results.

An aromatase inhibitor such as ? can be used to remove intratumoral estrogens. Systemic estrogen can be replaced, as desired, during the ADT phase of BAT with ?.
Various treatment combinations can be used in combination or in sequence with BAT. These include PARP inhibitors, immunotherapy, radiation therapy, and the meds Xtandi or Nubequa.

For more

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Russ’s book with detailed explanations, references, and programs is at: Amazon.com: Adaptive Bipolar Androgen Therapy (BAT) for Prostate Cancer eBook : Hollyer, Russ: Kindle Store. Free for Kindle Unlimited. Otherwise the Amazon minimum charge of $2.

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Meeting Notes

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SUMMARY KEYWORDS

adt, testosterone, androgen, bat, lupron, work, psa, cells, estrogen, good, hormone sensitive, trial, hormone, years, dht, sipping, therapy, prostate cancer, castrate, sensitive

SPEAKERS

Russ Hollyer (89%), Brian McCloskey (5%), Brad Power (3%), Jeffrey Dwyer (2%).

Session Outline

1. Introduction to today’s episode. (0:00)
2. Hormone sensitive androgens. (4:39)
3. Batman’s mask is unveiled. (9:34)
4. Denmeade’s statements on castrate resistant vs. hormone sensitive men. (13:36)
5. Castrate resistant vs. ADT. (19:35)
6. How do you persuade your oncologist to consider BAT? (25:13)
7. How did you become interested in cancer and hormones? (29:48)
8. How do you measure testosterone? (35:05)
9. Monitoring your testosterone levels. (39:38)
10. Genetic determinants of PSA response. (44:46)
11. How to use Olaparib to treat prostate cancer? (50:42)
12. Radiotherapy and androgen deprivation therapy. (54:50)

Brian McCloskey 0:00
Thanks everyone for joining the Prostate Cancer Lab. Today we have a special guest, Russ Hollyer. He's a member, and he is an expert in bipolar androgen therapy (BAT). He is an advanced prostate cancer patient and has really chartered new ground in terms of knowledge around bipolar androgen therapy. There's a lot of interest in bipolar androgen therapy from many of our patients that join our community, and Russ is truly an expert, and he's brought expert physicians to speak to us as recently, such as Emmanuel Antonarakis. Russ has a wealth of knowledge, and I know that you're going to get a lot from this session.

Russ Hollyer 0:58
A little about me. I'm Gleason 9 as diagnosed five years ago - T3c N1M0. I'm still hormone sensitive.

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First, “What is prostate cancer?” Well, it has four main types of cells. We know of more than 200 different cell lines, and with mutations and up-regulations, there are perhaps billions in total of different varieties.

PCa is heterogenous and is usually comprised of four cell types:

(A) HSPC Androgen Sensitive: Relies on external DHT to live. These are easily treated by ADT.

(B) CRPC Androgen Sensitive: Relies on DHT to live but has upregulated and/or mutated ARs so that it is more efficient at collecting DHT.

(C) CRPC Androgen Sensitive: Relies on DHT to live but can produce it internally if needed. These cells might be able to convert adrenal androgens into DHT (DHEA, DHEAS, androstenedione delta 4).

(D) CRPC Androgen Insensitive: Does not need DHT to live. These cells are very difficult to control and can morph into NEPC and small cell varieties.

When we use ADT, the goal is to drive testosterone down as low as possible. This deprives (A) of “fuel”.

Initially this appears to be successful. Usually in the early stages of PCa most cancer cells are (A) and most of them die when androgens are withheld. We are HSPC.

However, as (A) are killed, (B) and (C) start to grow and (D) will make an appearance. Eventually, the cancer is comprised primarily of cells that can live in low androgen conditions (CRPC).

The change from HSPC to CRPC typically takes 1-4 years. When PCa is CRPC or beyond it becomes much harder to control. If you have CRPC you can use hormones to shift the population back to (A). Clinical trials are showing us that by using BAT most patients can restore their sensitivity to ARB/ARSIs.

For hormonal purposes we can place them into four different categories.

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A. Category A - Hormone sensitive prostate cancer (HSPC) - the androgen sensitive cells that can be treated using androgen deprivation therapy (ADT).
B. Category B - They are androgen sensitive cells but are resistant to ADT. They upregulate or mutate their androgen receptors (ARs) so they can be more efficient, to get testosterone (DHT) a little easier. And what you can do with ADT, you can add in Xtandi or darolutamide. And that's going to lower the bar and make it harder for those guys to live. It lowers the bar for testosterone or androgens, and those guys have to upregulate their androgen receptors even more, which they will do.
C. Category C - They are androgen sensitive cells that require testosterone (DHT), but they can produce it internally. That's where Zytiga comes in. It blocks internal production through Cyp17. We think these cells can produce DHT from other androgens instead of testosterone and a conversion of DHEA, DHEAs (which comes out of DHEA) and androstenedione. Again, Zytiga blocks all of those.
D. Category D - CRPC androgen insensitive.

The rub for category B cells is that, while Xtandi or darolutamide will take the threshold down, eventually the upregulation of androgen receptors (ARs) is going to be high enough to get around this. In a similar way, you can control category C: you can block those through Zytiga. But eventually, those cells are going to die off, and then the type B's and D’s are going to predominate. The D’s are very hard to control. They're androgen insensitive, and BAT doesn't control these cells.

Doctors practice ADT, but the typical HSPC->CRPC change occurs in about one to four years. Some guys last only six months on it. Some guys last for four years, some guys last for over 10 years. As far as I know there is no good predictions of who's gonna last longer. So six months seems to be the maximum time that I'd want to be on ADT. I was on it for four and a half months.

If you are CRPC, trials are showing us that we could potentially use BAT to reset sensitivity back to sort of a hormone sensitive phenotype where Xtandi is going to work or darolutamide or possibly even just ADT.

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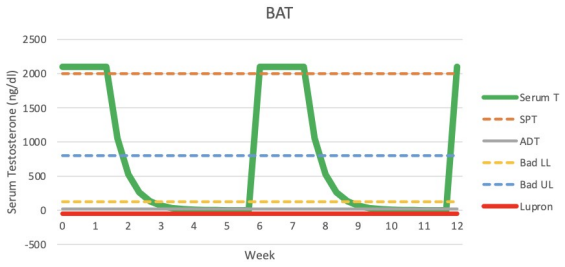
BAT has two parts

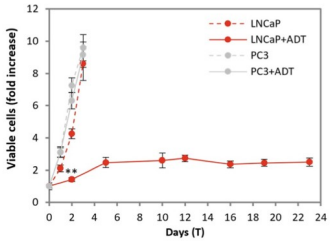
1. Rapidly increasing our androgens to a very high level (SPA). This increase makes the upregulated ARs of (B) a liability. Some of the mutations of (B) also become liabilities. SPA also induces DNA double strand breaks (DNA DSBs) and these serve to kill (A), (B), and (C).

If cancer cells are exposed to SPA for too long, (A) begins to dominate (they are dominant in HSPC men and present in smaller amounts in CRPC men).

Before this can happen, we move to part two.

2. Rapidly decrease our systemic androgens to a very low level (ADT). This environment controls cancer cells that require androgens for food (A and to a far lesser extent, B and C). This is particularly effective for HSPC men. Note that this requires some type of medical or physical castration.





BAT has two main parts. The first part is you take your antigens to very high levels, and they're called supraphysiological androgens, or SPA. And really we're talking DHT here because although testosterone does a lot of the work through the membrane androgen receptors, DHT works through the intracellular androgen receptors and eventually goes to the nuclear androgen receptors. Because DHT is perhaps the more important androgen, what researchers frequently do is to look at R1881 or DHT itself. R1881 is very similar to DHT. But it doesn't convert into estrogens. So it's very clean. Researchers have found that when we increase our DHT levels, we increase the DNA double strand breaks. One double strand break if it's unrepaired can cause apoptosis and the cancer cell is going to commit suicide or go into a senescent state.

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Bipolar Androgen Therapy (BAT)

PCa is heterogenous and is usually comprised of four cell types:

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BAT has two parts

1. Rapidly increasing our androgens to a very high level (SPA). This increase makes the upregulated ARs of (B) a liability. Some of the mutations of (B) also become liabilities. SPA also induces DNA double strand breaks (DNA DSBs) and these serve to kill (A), (B), and (C).

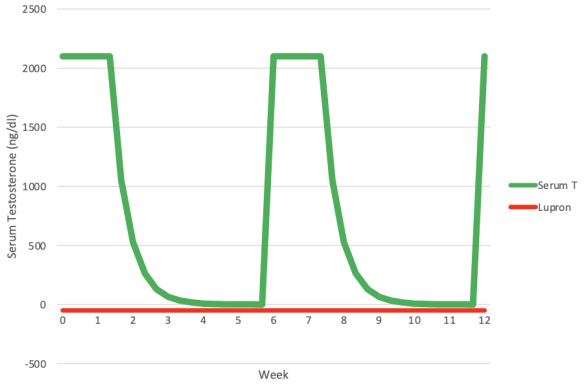
Drugs required:
Testosterone (propionate IM or Androgel are best)

If cancer cells are exposed to SPA for too long, (A) begins to dominate (they are dominant in HSPC men and present in smaller amounts in CRPC men). Before this can happen, we move to part two.

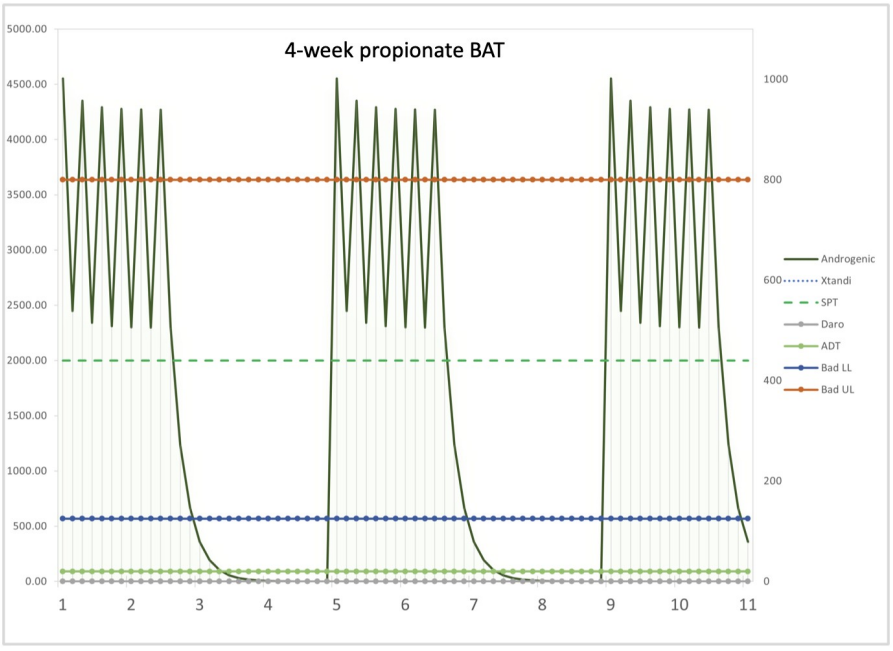
2. Rapidly decrease our systemic androgens to a very low level (ADT). This environment controls cancer cells that require androgens for food (A and to a far lesser extent, B and C). This is particularly effective for HSPC men. Note that this requires some type of medical or physical castration.

Drugs required:
Lupron or another form of ADT

Note that other drugs can be used to optimize BAT



So you might think, Okay, well, we could just do the SPA continuously. I did that for two years, actually. And it worked well for two years. But at some point in time, the androgen sensitive cells, HSPC cells, are going to start to dominate. They're growing and they're going to dominate and I think that's what happened to me and my PSA started to rise a little bit. We'll get to a chart later we can see that but before that can happen, we go to step two (ADT).



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The chart shows a testosterone formulation with a one day half life and that is what testosterone propionate has. So we can take our androgens very high and then very quickly take them low to a true castrate level. And this is a difference with propionate vs. cypionate. 400 mg of cypionate will not get down to a castrate level in a month; it will just slowly decay. It always is in a bad zone here and never gets done the castrate level so it doesn't really work very well on hormone sensitive guys. It might be okay for CRPC men since they might not need to go to castrate T levels.
The next chart shows hormone sensitive cell control using androgen ablation (ADT). It maintains control of those cells but has no effect on a CRPC cell line. If we do this long enough the HSPC cells are going to take off and the reason they're going to take off is because they're up regulating to become B's and C's and D cells.

One clinical trial was done in hormone sensitive men. It's called BATMAN.
The type A cells are going to be inhibited about 20-21% In three days of super physiological level DHT. Some of the CRPC cells are going to be inhibited 31%-38% in three days with the same level of DHT. However, while it is true that they are inhibited more than the HSPC cells, it is also true that some CRPC cells are not going to be inhibited at all. And what we need to remember is there's actually two phases here. So you're going to eventually drop down to an ADT level, then your HSPC cells are going to be inhibited greatly. And your CRPC cells as we know are not inhibited much at all and completely androgen insensitive cells are not inhibited at all.

One of the known mechanisms of BAT is that ADT up regulates ARs and then SPA causes a down regulation. So they become sort of like HSPC cells. And that continues to work for many men. So we're not seeing a failure due to people going HSPC, we're seeing a failure when androgen insensitive cells appear. And those are CRPC cells and not HSPC cells.
In my personal experience, I'm hormone sensitive. I'm still hormone sensitive, it's been almost five years now. When I started BAT almost 2 years ago, my PSA was 0.17 and it was slowly rising. And after 16 months, my PSA was 0.02 (after 18 months it started to rise and pBAT could be beginning to fail). So my experience doesn't tell me that doesn't work for HSPC men. However, if cypionate is used for monthly cycles I feel that it might be true that it will not work well for HSPC men. But if we use darolutamide, or extend the cycles, we don't have the same conditions or constraints on it. Better yet is to use testosterone propionate.

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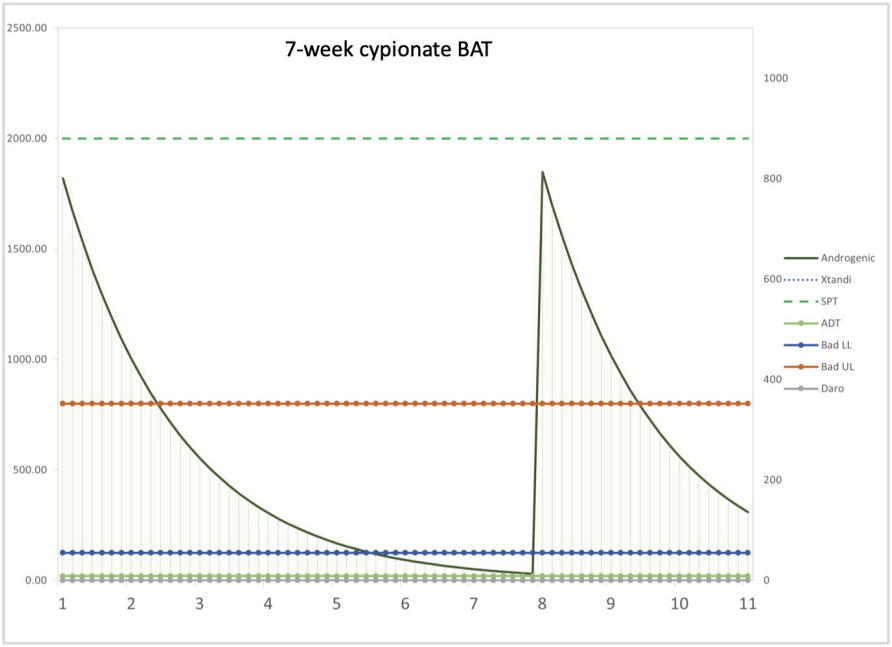

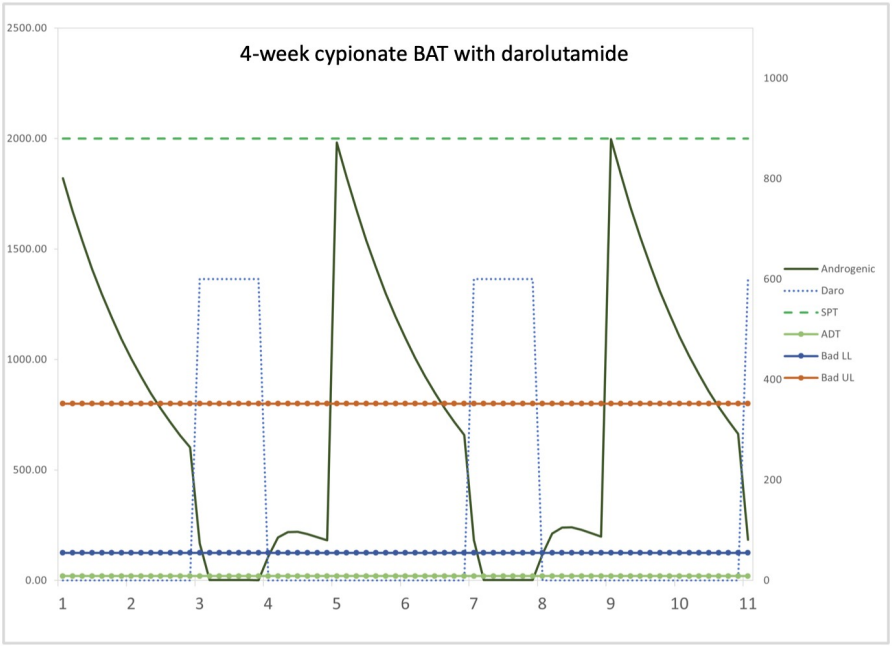

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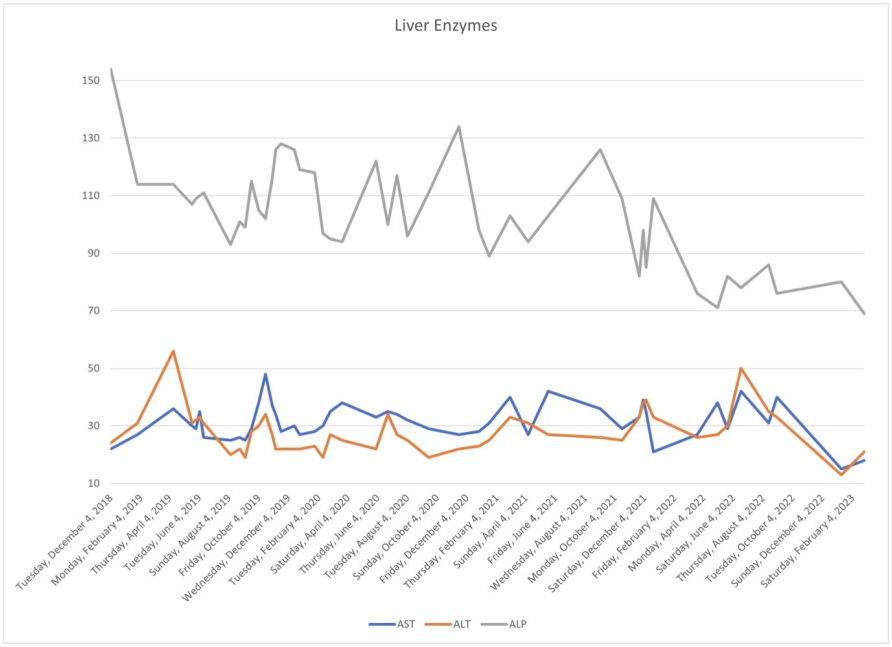

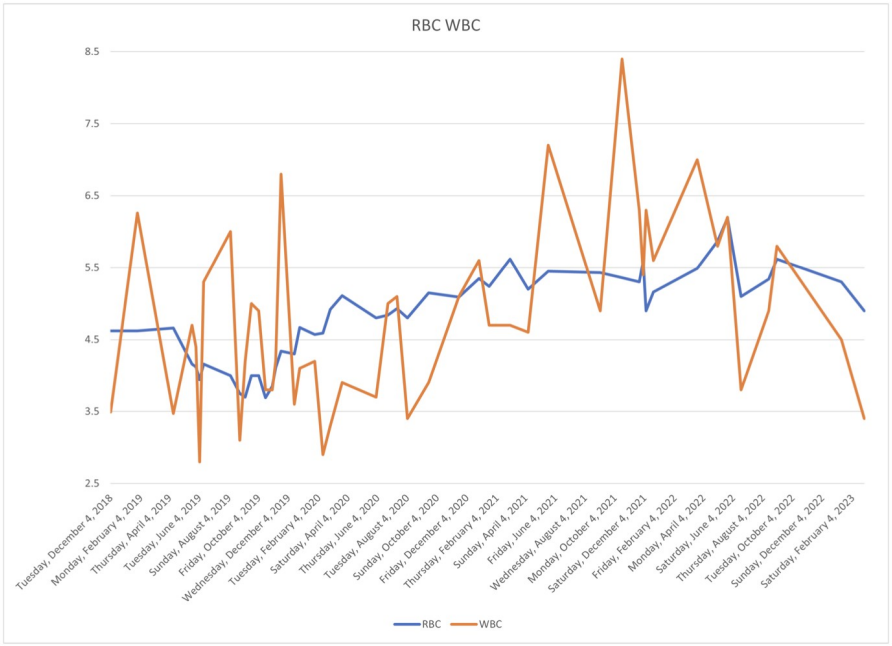

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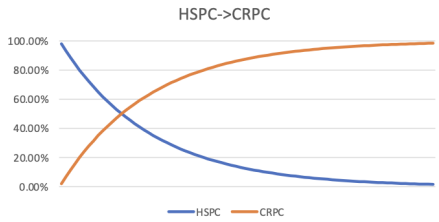
HSPC vs. CRPC

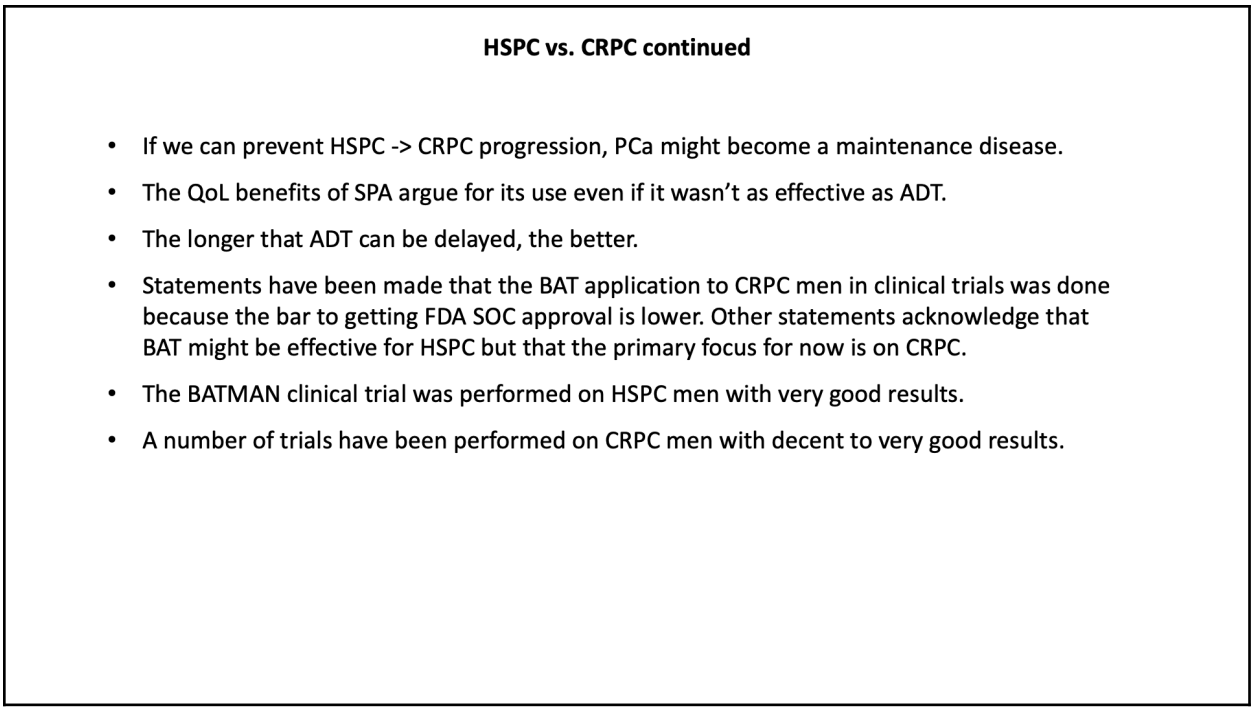
- SPA effectively inhibits growth of some CRPC cells (growth repression 3 days of 10 nM DHT 31-38%); cell/rat studies show that HSPC-like LNCaP cells are still inhibited in a dose dependent manner (growth repression 3 days of 10 nM DHT 21%). And some CRPC cells are not inhibited by SPA. HSPC appears to be “in the middle”.
- SPA mediated cell inhibition is greater in some CRPC cells than in HSPC cells but BAT consists of two phases. If a true castrate level is obtained in the second phase, inhibition is far greater in HSPC cells than in CRPC cells. Note: 4-week 400 mg cypionate cycles will never achieve true castrate levels.
- One of the known mechanisms of BAT is a down-regulation in ARs. However, BAT continues to work for many men. It appears that failure results, in part, when certain androgen insensitive cells appear. These are CRPC cells and not HSPC cells.
- I am HSPC. When I started BAT in 2021 my PSA was 0.17 and rising. After 16 months of BAT my PSA was 0.02. After 4 ½ years of BAT like maneuvers I am still HSPC.
- The HSPC -> CRPC transition is not digital. We do not know where the threshold of SPA repression lies. We need active ARs. HSPC cells have active ARs.



We do not know where the transition lies between HSPC turning into castrate resistant cells. It's not a digital event. It's an analog event. The chart is a crude depiction of your castrate resistant cells increasing over time and your hormone sensitive cells decreasing during ADT. We don't know what the optimum time is to start BAT. It would be difficult to perform such a trial.

Jeffrey Dwyer 13:23
Isn't Dr. Denmeade saying that he doesn't want people that are hormone sensitive doing that?

Russ Hollyer 13:36
Yes. I don't agree. But with 4 week cycles of cypionate, he has a valid point. I’d like to see a trial of 4 week cycles of cypionate used on HSPC men. I’m not sure if we’re going to see such a trial though.



Okay, on the next slide here, these are these statements so that the statements bullet for those were made by Denmeade.

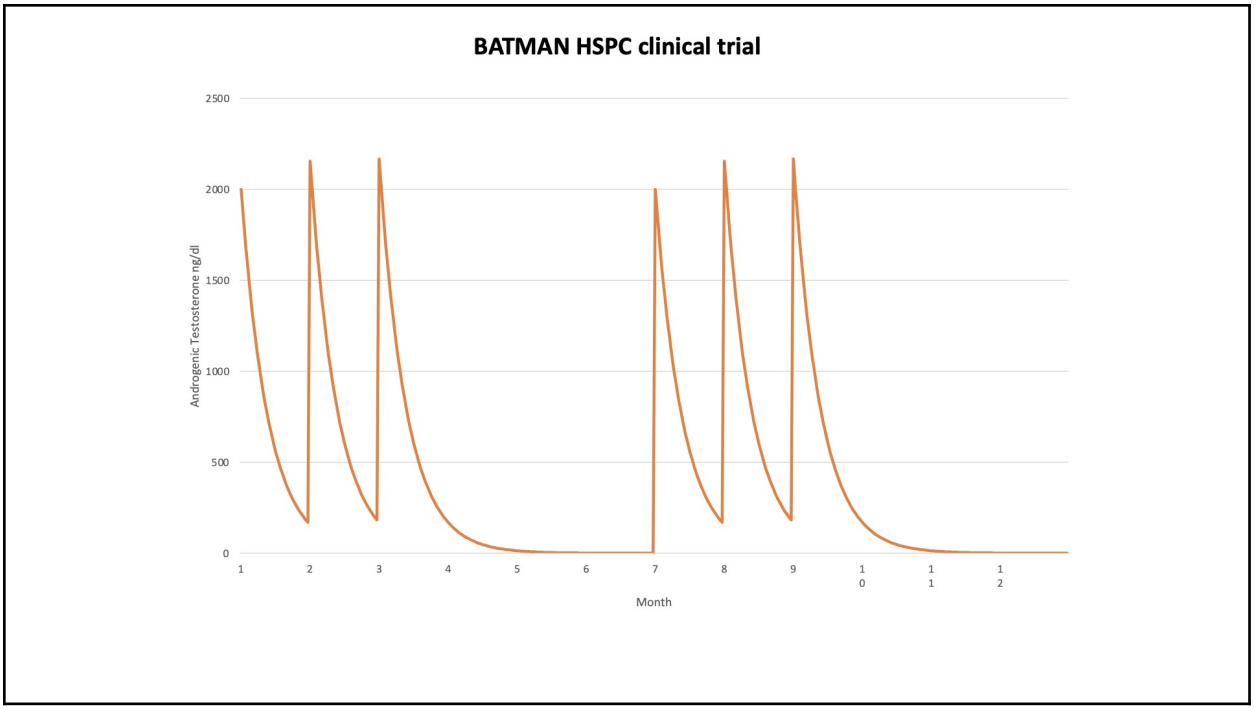
Jeff Dwyer 14:02
His colleagues that spoke to us last week – who was that?

Russ Hollyer 14:07
Yeah, Antonarakis. He works with Denmeade.

Jeff Dwyer 14:11
Neither one of them wanted castrate sensitive men to do it. As I understood it.

Russ Hollyer 14:23
Yes. That is their opinion. Denmeade made a comment a few years ago. In an interview he said the reason he chose castrate resistant rather than hormone sensitive was because the bar for approval was easier. He did not mention efficacy. He did not talk about whether it works or doesn't work. I don't think he would have made that statement if he knew that it's never going to work for hormone sensitive men.

“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]



Another thing he said recently is that BAT may or may not be effective for HSPC men. When he was questioned about the BATMAN trial, which is an HSPC trial, he said that the focus is on CRPC at this point in time.
I think his statements are motivated by getting into the approved standard of care. And if you're trying to get something approved for standard of care, we have lots of options for hormone sensitive guys. For example we have ADT which we know works well for a while. Eventually, it stops working, and that's a problem with it. Another is QoL. For CRPC, we don't have as many good options. And the longer it goes, the worse our options or the fewer options we have.
He knows this and that's I believe that's why he's trying to get into the CRPC space or why he said he was. And with cypionate, you're never going down to true castrate level or hormone ablation level. And because of that, I don't know if cypionate is ever going to work optimally on HSPC men.
If you recall the presentation by Antonarakis, another thing they're looking at is combination or sequential therapies.
What's been pursued so far is using BAT as a monotherapy. And I don't know if BAT monotherapy is going to be accepted for SOC by the FDA. I think that the most we're going to see, as Antonarakis said, we're going to see that it can be equivalent to other monotherapies, but not necessarily better. The quality of life, though, is going to be far improved. And if we look at it in sequence, like with Xtandi, using BAT to failure, and then using Xtandi, we see massive improvements.

Moving on to this, this will help clarify your question or answer your question. If you look at the BATMAN clinical trial, it worked well. And it was on HSPC men. What they did is they interleaved 3 cycles of testosterone cypionate monthly with 3 months of ADT. With 4-week 400 mg cypionate injections, we're not getting down very low in testosterone, it gets down to about

100-200. But by stopping entirely for three months, we get down to a true castrate level. And at that point in time, we are getting real control of these hormone sensitive men. So this is one option that can be pursued. If you're hormone sensitive, you could follow a scheme like the Batman trial. There's other ways you could do it, but this is one of them. Does that answer your question?

Jeff Dwyer 19:09
I think so. Because what I'm trying to what I'm trying to figure out is, it seems to be when it's presented by people, when I've heard about it, it's I presented as a Hail Mary end of the road treatment, when everything else fails for castrate resistant men, and it doesn't get presented as monotherapy or as the Batman is presented. You don't hear about it. You know?

Russ Hollyer 19:37
I think that's mostly the MO’s who are presenting it. I believe it's political. They're trying to get into castrate resistant space or trying to get BAT approved as a standard of care treatment for that.
If we look at BATMAN, for example, one thing that's missing from this equation that we're not really discussing is quality of life (QOL) : libido, muscle, bone health, mental health are very much improved with BAT.

So even if the efficacy is the same as ADT, you have to look at the quality of life aspect too and say, “Well, which would you prefer: ADT which means no libido, muscle loss, fat gain, bone mineral density loss, and hot flashes versus using BAT, which doesn't have any of those negative QOL issues? And it’s actually going to reverse some of those issues.”
You have to look at and say, “Well, what do I want to do? If I have option A, which is going to last, say, 10 years, and Option B, which is going to last for 10 years. So either way I can live for 10 years. But if I use Option A I live, healthy, happy 50% of the time, and maybe not so happy 50% of the time, versus option B, where I'm pretty much miserable 100% of the time.” For me the choice was clear: I have to pick the one where I feel better for 50% of time.

And if we look at bone health, and muscle health, those are very highly correlated with prostate cancer mortality and progression. We look at those two aspects and BAT presents some positive alterations of QOL. In addition, we see that we're not only going to have better results, or maybe we have the same results from the prostate cancer aspect, we're going to get better results for cardiac risk, for less fracture risk, less sarcopenia risk. We have better results from other risk factors. So, I'm looking at that and say, “I'm gonna feel better for half the time. And I'm going to live just as long.” And I think what we're seeing is you might be able to live longer with it. And I'm going to reduce my risk factors from other health issues.

Brian McCloskey 22:45
For those that are considering that in a hormone sensitive setting. Do you have any data that would help patients understand those that are better qualified for it versus those that are not? For example, in castration resistant, we're looking at high AR, TP53, or looking at BRCA. Are

there any leading indicators for patients who are in a hormone-sensitive setting that they will respond better than others?

Russ Hollyer 23:22
Unfortunately none that I know of. For CRPC we have a lot of data. I know what you're asking for, and it makes sense. You want to see the data. Well, who's going to be on that top end of the longevity curve, and who gets the most benefit, and who gets the least benefit? I don't think we have that data for HSPC yet. They're doing a lot of the trials and studies and focus on the CRPC space. And so we have a lot of data in CRPC. They're trying to flesh out specifically who's going to benefit, and who is not, or at least we don’t know that information yet.

Brian McCloskey 24:15
That's an opportunity.

Russ Hollyer 24:18
It's an opportunity. Definitely, certainly a big opportunity. Why did I respond? I'd love to know why I responded. It'd be nice to know. That'd be for 20/20 hindsight, but it can help a lot of others.

Brian McCloskey 24:32
Do you have TP53?

Russ Hollyer 24:35
I do not have any mutations whatsoever. After my original surgery, Tempus picked up some mutations, but Guardant’s CD X test didn’t show any mutations and I've had some other genomic tests. There are supposedly no mutations now and MSI is stable and tumor metabolic burden has been dropping according to Guardant.

Brad Power 25:21
Off of the science and more on the access to this: Russ, what kind of relationship do you have with your oncologist? I could be sitting in the shoes of many of the people here and say, “I buy everything. You're running experiments on yourself. You have a model and a theory for why it's doing what it's doing and why you're able to tune it. And it's wonderful. And I want that too.” But then along the lines of what Brian was saying, “What evidence is there?” Because a typical oncologist is going to want research results or something. So how do you persuade them? What do you present to your oncologist?

Russ Hollyer 26:08
Very good question. My oncologist and I have a good relationship. I've known her for over four and a half years now. And she has watched me do these different things like high estrogen for ADT. At first she didn't think it would work but it worked well.
But more to your point, realistically, like what do you do? What do you do with an MO who is not necessarily as understanding as mine. For the CRPC space, I believe we do have good data

and Denmeade, for example, is willing to talk to your MO to help them conduct BAT. So for this setting we have some defined resources.
But if you're hormone sensitive, we don't have the resources, or the research to support it. And I don't think you can go into your MO and say, Yeah, Russ does it. I think they're just going to kind of laugh.
What I do with my BAT program is to get drugs from my NMD, my naturopathic medical doctor, I tell him what I want and show him data to support my request. My MO monitors my progress, and I have assured her that I will follow her advice if BAT fails.

Brad Power 28:54
You're a citizen scientist, a role model for people who are going to be actively engaged in their care. You're the extreme version of someone who's really taken full responsibility for their care. And your oncologist is following your lead. You're not the copilot, you're the pilot. And that's very amazing. What gives you the confidence to do that? What is your background? Who is Russ Hollyer, and why is he willing to go out on a limb and work on his own personalized treatment and figure out what's working for him and run experiments on himself?

Russ Hollyer 29:42
I'm an electrical engineer. I did very well in school and worked for a medical company. I have a lot of experience with dealing with the FDA, and that's pretty much what my job was doing; interfacing with the FDA, designing quality screens, and data analysis, and along the way, I picked up a lot of tools for analyzing data and looking into and working on medical products, not necessarily cancer-related, but it wasn't that difficult to segue into cancer.

Over the years, now over four decades, I have been interested in hormones. Prostate cancer is a hormonal cancer, one of the few that we know of.
Five years ago, when I started talking to doctors about ADT, I was told to use a GNrH agonist, Lupron. So I looked into Lupron, and I said, “Okay, there is bone health risk and cardiac risk. And obviously, you're taking your estrogen down to zero along with your testosterone.” So I started talking to doctors about using estrogen, high dose estrogen, which I knew should drop my testosterone close to zero. What I found is that when I talked to four different MOs, none of them thought it would work. Three of them thought it wouldn’t reduce my testosterone, the fourth one thought it would reduce it but maybe not enough. Her words were: “I think it's going to reduce your testosterone, but my fear is it might not do it well enough.” That was realistic and based on the sparsity of data, very understandable. And she's my girl. She's been my MO ever since because she actually understood what I was doing, and she showed she had an understanding of hormones.
I very early on came to the conclusion that many doctors don't seem to know much more than me. And in this particular case, they didn't seem to know what I feel that I know. So I was comfortable about guiding my therapies to an extent.
I also applied a test from my background in quality screening test experience. I'm very comfortable with testing things out on myself and trying to analyze the results. I'm fairly comfortable with looking at different trials.

“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]

Brad Power 33:09
Picking up on that last point: What are the tests that you're using that give you confidence you're keeping in the guardrails, that you're not risking your health, and you're in a safe zone. What are the tests that you are using to monitor your progress?

Russ Hollyer 33:30
The very crude one is PSA. I can compare PSA readings in the same hormonal environment (High androgens will overexpress PSA it and lack of androgens or Xtandi, for example, will under-express it about 90%). But I will test PSA in the same environment. Like towards the end of the cycle to get a good feel for how PSA or KLK3 is expressing itself over time. But what I do when my insurance will allow me (about once every six months or so), I do a PSA PET scan. And that gives me a good feel for what's going on. And I believe it's once every three months they will allow a Guardant 360 CD X test which is nice so that I can keep a track of my mutations and my tumor metabolic burden, and MSI status. By the way they don't give me any analog results. I'm going to talk to my MO about that. But I suspect the reason why I don't get any analog results is simply because there's not much to see. But those are the three tests and I look at blood tests CMP, CBC, liver enzyme trends over time, kidney health, hematocrit, various other parameters. The most important one IMO is PSMA-PET scans.

Brad Power 35:08
And this testosterone like on this slide that you have up here there tractor tracking testosterone or androgen? Is that just a blood test you're getting every week? Or how does that work?

Russ Hollyer 35:17
With testosterone and the androgenic levels of it, we can calculate levels from the halflife and the bioavailability of it. And we can calculate what your serum testosterone levels are going to be hypothetically. Many trials and experiments and studies have been done over the years to show us how it works in most men.
But these are levels for other men and not me. So what I have done using cypionate is measure my serum levels about once a month. And they all correlated.
It got to the point that I could tell my MO what my testosterone was. I didn’t have to measure. I recall one time she asked, and I told her that I just had my testosterone measured, and when I get the results back, they're gonna be around 1825. A few days later I received the results. It was 1828.
We’re all a little bit different. But these curves are pretty darn close to what you're gonna see. What I like to do is occasionally measure a couple of points and calculate the half-life and serum max. I’ve done these characterizations for cypionate, propionate, various gels and orals.
I also measure occasionally when I’m supposedly castrate to make sure that I actually am going to this nice low level. And that tells me that Lupron in my case is effective, that my own body's testosterone is not gumming up the works. If you produce testosterone you're always gonna have to be on Lupron or be taking Orgovyx or another form of ADT. If you don't do that, your body's testosterone is going to take over. If your body's testosterone is 500, you're going to see testosterone only go down to 500. This is going to defeat BAT.

Unknown Speaker 37:31
And you use estrogen for it?

Russ Hollyer 37:35
I used high dose estrogen for ADT, to reduce my testosterone to zero, but it doesn't play well with BAT. And the reason why it doesn't work well with it is because, while it takes less than a week to wash out of your system, it takes about three or four weeks to drop your testosterone down to zero. And we don't want our testosterone and our estrogen to be high at the same time. Friedman is coming up to speak to us later this week. He's very smart and he's done a lot of research in that area.
I'd love to use high estrogen but I can't use it with BAT. So I use it for standalone ADT. However, I use a low dose estrogen patch to replace estrogen during my ADT phase (or an estriol cream). I'm not worried about dropping my testosterone down with it.

Jeff Dwyer 39:14
You could stay on high dose estrogen for your ADT until you appear to be castrate resistant, and then you would transfer to BAT, but you'd have to use a different ADT drug. You couldn't use high dose estrogen at that point.

Russ Hollyer 39:36
Yes. One thing that my MO and I did, and this was her suggestion (not for the first time, I was pleasantly surprised by one of her suggestions). We monitored my testosterone, and I didn't get a Lupron shot for the first three months on BAT. My body’s testosterone production was zero. If you use Lupron, it's going to take months for testosterone to recover. I was doing high dose testosterone. So my endogenous or my body's testosterone was shut off. And when I stopped SPA and started BAT, she said, “We don't want you to deal with drugs that you don’t need. So we could just monitor your testosterone.” I said, “Okay, that's great.” So if you're doing high dose estrogen right now, when you go off estrogen, you might be able to monitor testosterone for a while before you start to worry about doing Lupron shots or Firmagon or Orgovyx. I think Orgovyx is going to be the best one. It's oral. And I think it's gonna be the best one because it drops your testosterone down pretty quickly. And your testosterone recovers fast after you're done. It has a fairly short half life and I think it's good. I think you actually work without using it full time during BAT. You could just use it when you want your testosterone to be zero or very low. Because you are controlling your testosterone exogenously through your shots. It won’t be an issue to have your body’s testosterone production low all the time and that's what they're doing in trials right now, what they've been doing in clinical studies like Lupron continuously. That’s what I do also. I use Lupron continuously.

“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]

Candidates for BAT

- HSPC men.
- Early CRPC.
- Possibly middle or late CRPC with some conditions.

Disqualifiers:

- Symptomatic bone pain. You could make the pain worse.
- Bone mets that are close to the spine or are threatening a fracture. You could wind up with spinal cord compression or a fracture.
- If the prostate gland is bulky or a pelvic lymph node is close to obstructing your urinary tract, you could develop a renal obstruction or possibly even kidney failure.
- Genetic determinants of BAT response. The following mutation(s) have been displayed by extreme BAT responders:
  - BRCA2
  - TP53
  - TP53/BRCA2
  - TP53/ BARD1
  - BRCA2/ATM
  - ARID1A
  - ATM/RB1
  - CDK12 has some response.
  - CRPC men with homologous recombination repair (HRR) mutations had a 68% PSA response rate (any PSA reduction). Men without an HRR mutation had a 37% PSA response rate.
  - Men with tumor suppressor loss (TP53/PTEN, PTEN/RB1, TP53/RB1) exhibited a 54% PSA response rate.

Things to remember:

- If bone pain occurs, it is probably from inflammatory factors and not from cancer growth. Pain can be tested out using 300 mg of Androgel. If you have pain, Androgel will wash out in a few days.
- If muscle pain occurs, it can be reduced by using NSAIDs such as Ibuprofen or Aleve. You might need to use fairly high doses. Ibuprofen (Motrin) has a very short half-life so dosing might need to be done every 3 or 4 hours. Aleve has a much longer half-life, and you might find one or two doses a day will work.
- PSA might go up for a couple of months. This does not necessarily mean BAT is failing. Sometimes it takes time to work. Sometimes scans will be at odds with PSA. Always go with the scans. As Dr. Antonarakis mentioned, what makes it tricky is that sometimes PSA will increase for a couple of months and scans will also deteriorate. It then becomes a judgement call.

Russ Hollyer 42:10
I believe BAT is going to be best at HSPC but early CRPC is not going to be a bad time and that's what they're trying to do conventionally. You could possibly use BAT for middle or late CRPC but you're going to have to worry about some conditions.
These are the conditions.

- The first is symptomatic bone pain - if you have bone pain, you could make the pain worse. I believe there's a way to check it out though you can use Androgel. A very short burst of androgens will go through your system in a day or two. You don't have to wait for five weeks for cypionate. By the way the bone pain is not from cancer, it's from inflammation factors, according to Denmeade.
- The second condition is that if you have mets that are close to the bone and could make a fracture or really close to spinal cord those can be problematic and you might not want to exacerbate those whatsoever because you could get some some cancer growth and then you're gonna get regression and but in the mean when you get the growth then you could okay you have a fracture or spinal cord rupture.

Brian McCloskey 43:36
So just a point on that, Russ, is that if you have soft tissue meds only, you're probably not going to feel a lot of this. I'm a case in point. I just wash it. I felt it a little bit in my pelvis. But I didn't really feel it anywhere else.

Russ Hollyer 43:52
So you shouldn't feel it. However, I still think the best thing to do would just be to get some Androgel. It's available at most local pharmacies. 400 milligrams of Androgel and you're gonna be able to see if you have pain and if you can withstand it.

That's the approach that I would use.
There are genetic determinants of response. We know that HR or HRD or HRR mutations like BRCA2, TP53, etc., are good predictors. Those all have very good responses to BAT, about 68% PSA response, any PSA reduction. If you had a tumor suppressor mutation, you had about a 54% response rate.
I'm looking at any PSA reduction as good. I don't always look at the 50% mark that we like to see in clinical trials. I'm looking at whether or not I can use a therapy for two years and I don't get any progress of cancer. I'm saying okay, that's a win that's two extra years, two extra years of life.
I know a couple guys on here had muscle pain. I think it might be from the curve that cypionate gives you. But if you use ibuprofen or Aleve, they will very likely wipe out that pain. A problem with ibuprofen and Motrin is a very short half life. So you're gonna have to dose up multiple times during the day over and over and over and over every three, four hours. Aleve has a much longer half life. You might need to dose once or twice a day, it's going to be a lot easier to be taking Aleve, and you're gonna have to take a lot less of it than with ibuprofen or Motrin.

Brian McCloskey 46:37
If it works, for those that have kidney issues, you have to be careful with Motrin, Aleve. So just a warning. That just came from my nephrologist, just this week because I've got a kidney challenge now.

Russ Hollyer 47:01
Something to remember, which Antonarakis pointed out, is that PSA might go off for a couple months. In fact, your cancer scans might show that cancer is growing for a couple of months. That doesn't necessarily mean BAT is not working. It sometimes takes a few months for your PSA to go down or cancer to regress. That's the real conundrum is when your PSA is rising and your PSMA-PET scans are looking worse, then what do you do? Even after a few months? Well, you know it may reverse, but it might not. So that's where you're going to have to look at your clinical symptoms, talk to your MO, and decide if you're willing to take the risk of staying on it or not.

“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]

How I perform BAT

- Lupron continuously to reduce my body’s testosterone.
- Testosterone propionate injections to maintain an SPA level.

Optional:

- Continuously: Cabergoline to reduce prolactin.
- Continuously: Letrozole to reduce tumoral estrogen and estrogen converted from testosterone.
- SPT (phase 1): NPP injections on occasion for any joint issues.
- ADT (phase 2): SARMs such as Rad-140 during the ADT phase to maintain a weak anabolic environment.
- I sometimes introduce 1–2-day spikes of SPA. This can’t be done with cypionate. It is best accomplished with gels but can be done with propionate if darolutamide or another ARB/ARSI is used.
- Usually during ADT but sometimes during SPA: Occasional use of Zytiga and finasteride.
- ADT (phase 2): Estrogen patches (0.05-0.1 mg/day) to replace systemic estrogen.

- I am currently experimenting with olaparib to see how a short pulse performs with BAT.
- I am looking into other synergists and options. Sequentially or in combination with BAT. I have 30 backup plans as of today. Over half of them involve BAT or SPA.

This is how I performed BAT. I use Lupron continuously. This reduces my body's testosterone production. I use propionate injections to maintain the high level.
I use Cabergoline to reduce prolactin. And that I think is particularly important for castrate resistant men, but as far as I know, it has not been well tested in clinical trials. A lot of studies have shown that prolactin reduces your castrate resistant overall survival.
And I use letrozole or an aromatase inhibitor to reduce my tumor estrogen and any estrogen that is converted from testosterone. But then I replace a little bit of estrogen with estrogen patches when I am on ADT.
And then I use NPP, that's an anabolic steroid, for any kind of joint pains, so I feel really good during the high testosterone phase.
And in the ADT phase, I use SARMS (selective androgen receptor modulators) like rad 140 and so on. I prefer this to maintain a weak anabolic environment so that I don't see all my muscles and bones go in a bad direction, and I have a little bit of libido - I have a little bit of life left. While I'm waiting for the next high testosterone phase, and then based on animal research and cell research, I introduce a couple of short spikes of SPA, high androgens - you can't really do that with cypionate.
And during SPA and ADT I use finasteride on occasion, that is going to reduce systemic DHT. Zytiga is going to block testosterone biosynthesis from adrenals, tumor, and testes, and also biosynthesis from other sex hormones. I think that someday we might find that Zytiga plays well with BAT but not necessarily after BAT.

I'm always doing experiments, I'm looking into how olaparib plays with BAT. I did a short pulse of olaparib - I don't think we need to use it continuously. I think maybe a three or four day pulse started one day before your high testosterone spike, continuing for three days after your DNA

double strand breaks if they're not repaired within two or three days, apoptosis occurs. So I don't think we're going to need to use olaparib for a long time, I think just surrounding that pulse. And there's also darolutamide or Xtandi - those increase DNA double strand breaks too, so I plan to use it right at the end of my cycle, my high testosterone cyclorama are on right now for three or four days to again, hopefully synergize with the need to double strand breaks and inhibit NHEJ repair, and then push DNA-DSBs to the HR repair path, which should be swamped out. There are two types of repair for DNA double strand breaks, and if neither of them works, cancer cells die.

I used Xtandi for 3 weeks and my PSA dropped much more than I expected. Xtandi is harsh though and I didn’t like the side effects. I might try again with darolutamide. Fewer and less severe side effects.

I'm looking at a lot of other possibilities. As of this morning I had 32 backup plans. Maybe 25 of them involve BAT or SPA, and in large part it's because while many of them synergize with BAT, I want to add SPA pulses in so I feel good. BAT might work with radioligand therapy, but there are reasons it helps and there's a reason it hurts.

BAT should work well with regular radiotherapy and some types of chemo.

Potential BAT synergists

- PARP inhibitors (e.g., Olaparib). Based on the DNA-DSB repair time, the half-life of Olaparib, the induction time of DNA-DSBs via SPA, Olaparib should be an effective synergist if started the day prior to a high T spike and continued for a total of 4 days. Clinical trial NCT03516812. Results show good synergism, but the results are not enhanced with BRCA or HRR mutations.
- Immunotherapy (e.g., Nivolumab). Clinical trial COMBAT-CRPC (NCT03554317). Good results.
- 2023: Carboplatin. Clinical trial HI-TECH (NCT03522064).
- 2024: BAT and darolutamide interleaved. Clinical Trial ExBAT (NCT04558866)
- 2026: BAT and Xtandi interleaved. Clinical Trial STEP-UP (NCT04363164). RESTORE and TRANSFORMER delved into the use of Xtandi for sequential therapy. STEP-UP will examine repeats and two different approaches.
- 2027: Radium-223. Clinical trial BAT-RAD (NCT04704505).
- I think that we may find that the following can be used:
    1. Zytiga for the first week or two following SPA. Washout and CYP17 restoration might take 4-6 weeks. I am not sure how Zytiga will interact with SPA. It might be prudent to restrict Zytiga use to every 3rd or 4th cycle.
    2. Extremely high testosterone pulses. Cell damage does not appear to level off at doses of R1881 that are roughly the equivalent of 50,000 ng/dl of testosterone. I tried out a 10k ng/dl pulse and my PSA dropped from 1.49 to 0.15 after I was castrate for a single day. The following month I tried a 25k ng/dl pulse. My PSA did not drop nearly as much, and I suspect that I damaged my immune system.
    3. Very short testosterone pulses. Most DNA damage occurs within hours of SPA application (certain genetic changes occur within minutes). DNA damage returns to baseline after 24 hours or so of application. HSPC cells apparently require higher and shorter SPA pulses. However, it has also been observed that exposure to an SPA environment increases the synthesis and decreases the turnover of cellular AR proteins.

Here's a list of some clinical trials, PARP inhibitors, immunotherapy, and carboplatin. Another trial is ExBAT with BAT and darolutamide interleaved, that'll be interesting. And in 2026, this is a big one. The Step Up trial. And they're going to look at how Xtandi performs with that if that can resensitize us to Xtandi over and over and over and over. If they can desensitize this ad infinitum. Prostate cancer if you catch it at the early castrate resistant phase or the hormone sensitive phase, prostate cancer becomes like diabetes, it's a manageable disease so you just live with it. It requires a little more than diabetes for the treatment.

“How I Am Running Experiments on Myself to Control My Prostate Cancer – Using Bipolar Androgen Therapy” (Russ Hollyer) [#58]

Unknown Speaker 54:10
Who's running this one?

Russ Hollyer 54:12
Denmeade is the leader of the trial. The trial came out of his RESTORE and TRANSFORMER trials. He saw some interesting things about resensitization. I’m so glad that Denmeade is heading these trials. He is quick to seize on an opportunity and is a brilliant researcher. Anyway, he’s said in interviews, “Hey, I'm not sure how many times we can do this. Maybe we can do this over and over and over.” There's no reason why we can't think of, and if he's right, we have a whole new ballgame. It's a pretty large trial and if it works, I would hope that the FDA is going to fast track BAT/Xtandi because we're looking at a major improvement, a major game change.

And there's another one, BAT-RAD, which uses radium 223. And I believe that high testosterone pulses and ADT, will synergize very nicely with radiation therapies. I don't know about radioligand therapies quite as much. There's again, a con and a pro. We have data now that says that androgen deprivation therapy and high testosterone spikes will synergize with the double DNA double strand breaks of radiation therapy. If I do radiation therapy before the trial results, I am going to complement the radiation with BAT and some other suspected or known sensitizers/protectors. I won't wait for the clinical trial to be out. I might not have that luxury.
I suspect we’ll find out that darolutamide is resensitized similar to Xtandi. I could be wrong on that one though - they have different resistance mechanisms.
I do think that we will find that Xtandi or darolutamide work well when timed properly during the ADT phase. Darolutamide has more potential than Xtandi IMO because of a far shorter half-life, and fewer side effects.

We're going to find eventually that very high testosterone pulses are good, I don't know when we're going to find this out. Because right now we're using cypionate, and you can't do these very easily. Very short testosterone pulses might be helpful. DNA damage occurs rapidly, some genetic changes occur within 15 minutes, DNA damage occurs within 24 hours, 48 hours, maybe, at the most, if not repaired, boom, death. So I think we're gonna find that short testosterone pulses are very handy but again, with cypionate, we can't do these things. So we're gonna have to look at propionate or Androgel. They're doing an Androgel trial right now, but they aren’t dosing high enough to get to SPA levels. But it might open the door to more trials of Androgel.

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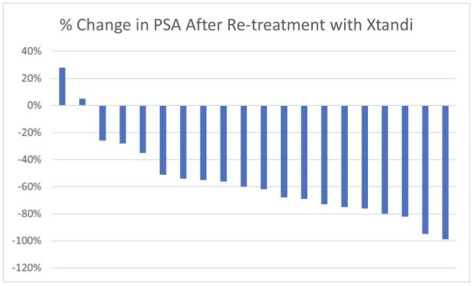
Data from CRPC men in the RESTORE clinical trial
BAT was executed first. Regardless of whether it was useful as a monotherapy, men who had previously failed Xtandi were rechallenged with Xtandi.



TRANSFORMER showed us that **over 75% of CRPC patients who had failed Zytiga and were subsequently treated with BAT had a PSA50 response when treated with Xtandi. This was about 3 times the typical Xtandi post Zytiga failure response rate.**

Here's some data from RESTORE. If we do BAT and then rechallenge with Xtandi, we see very nice efficacy of Xtandi at that point. Transformer, over 75% of CRPC men who had failed Zytiga went through BAT and then used Xtandi had a response. And many of the responses were not minimal. For the most part, they were pretty good responses because some of them lasted for years. If we look at the data that the FDA originally looked at to approve Xtandi on CRPC men and hormone sensitive men, we're looking at it working much longer and with much more efficacy if BAT is used first.

Russ Hollyer 59:30
I'd be willing to come back and talk again. We’ve talked a lot about bone density. Some guys have bone density issues, my bone density increased 5.2% in a year and a half according to a DEXA BMD. I thought that those numbers were crazy so I had a DEXA fit scan. It showed a 4% bone density increase but measured more points and so is more accurate, and it also showed an overall bone mass increase of 4%.

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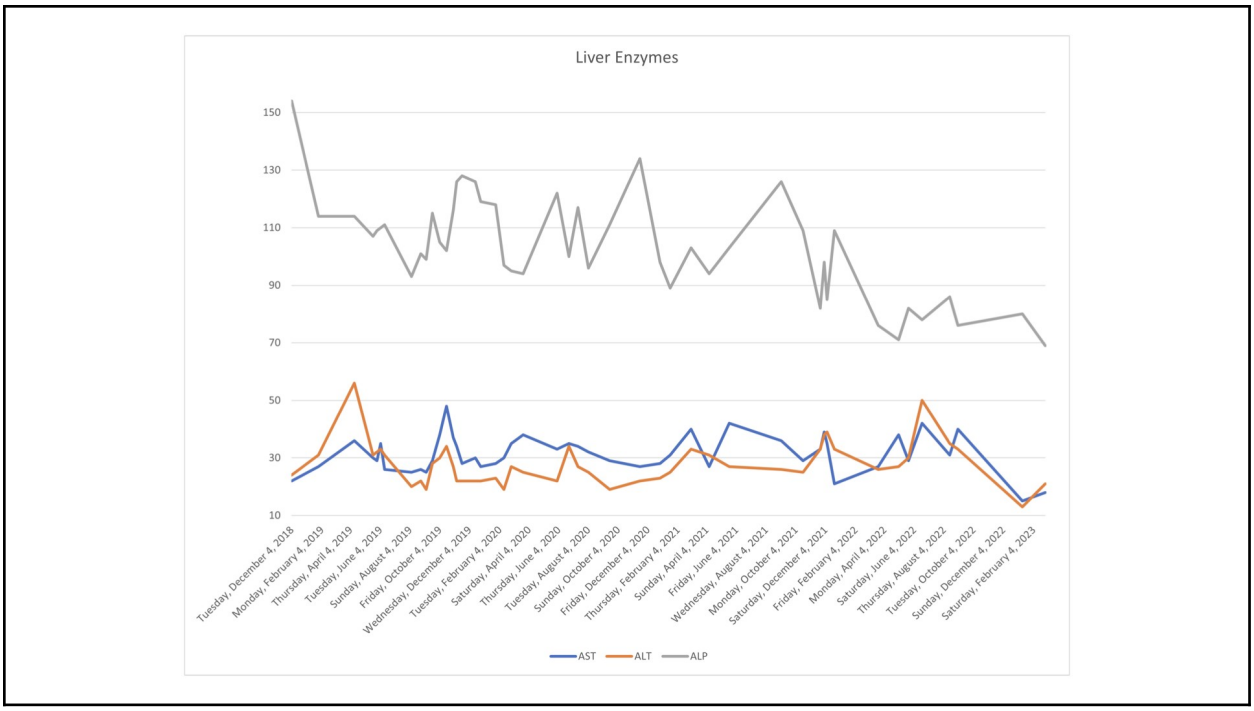
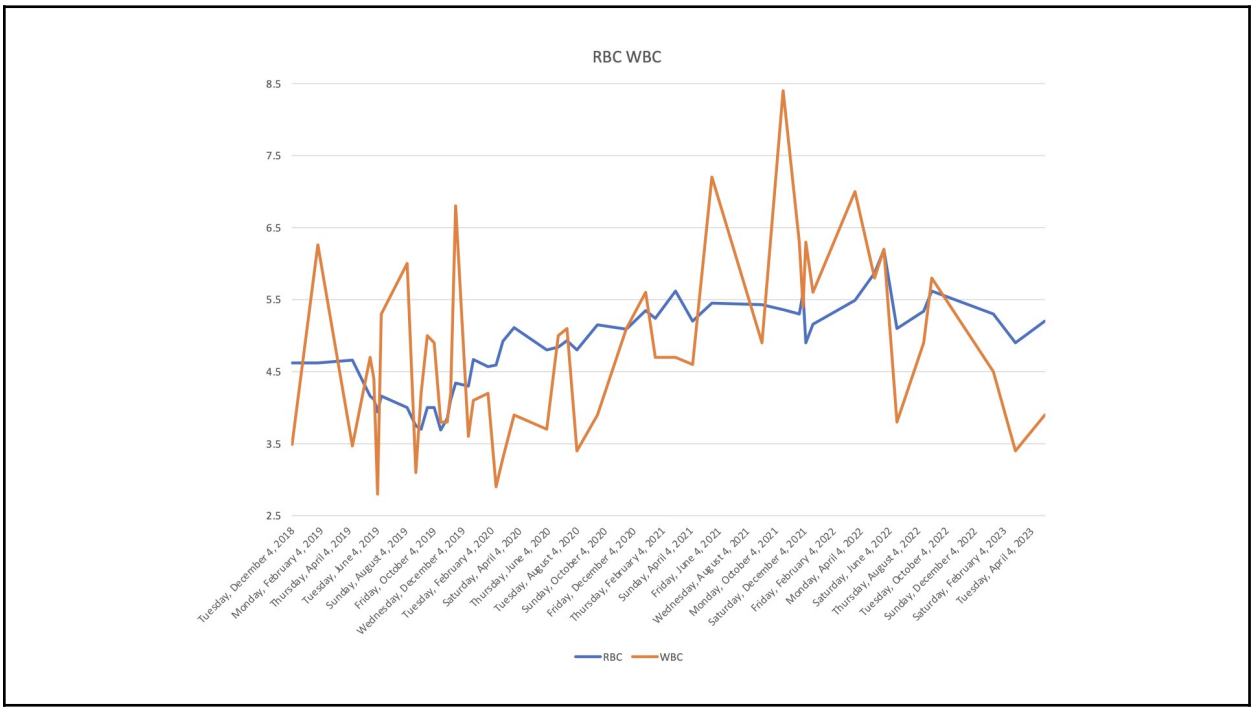


My liver enzymes have gone down.



My white blood cells and red blood cells are holding about the same.

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Androgens

1. Increase sex drive
2. Increase muscle mass and strength
3. Improve memory and alleviate depression
4. Decrease fatigue
5. Increase bone mass
6. Increase hematocrit and RBC (this needs to be monitored)
7. Decrease systemic immune response. However, SPA increases immune factors in cancer cells.

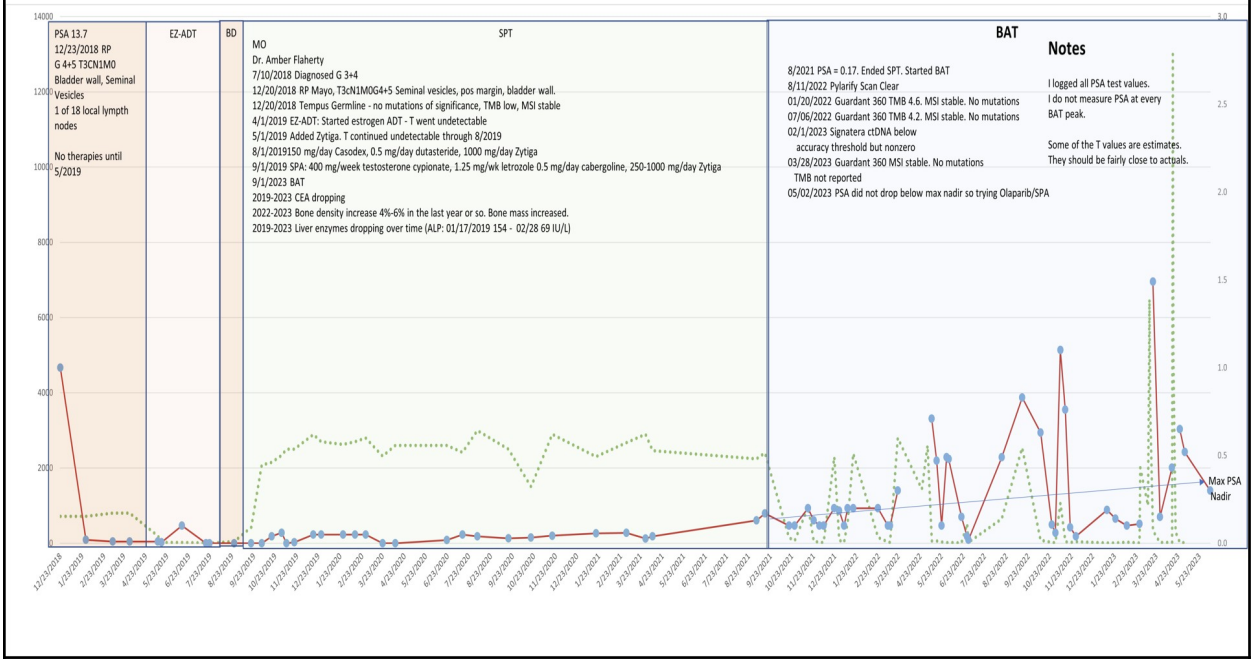
As of 5/17/2023

Time on BAT 613 days

Lean mass change 15.5 lbs.
Fat change -1.38%

Bone density change as of 8/2022: +5.20%. A separate test (DEXA-FIT) showed a 4.0% bone density increase as well as an overall bone mass increase of 4.8%.

ALP 126->80
ALT 26->17
AST 36->20
WBC 4.9->3.9
RBC 5.43->5.19



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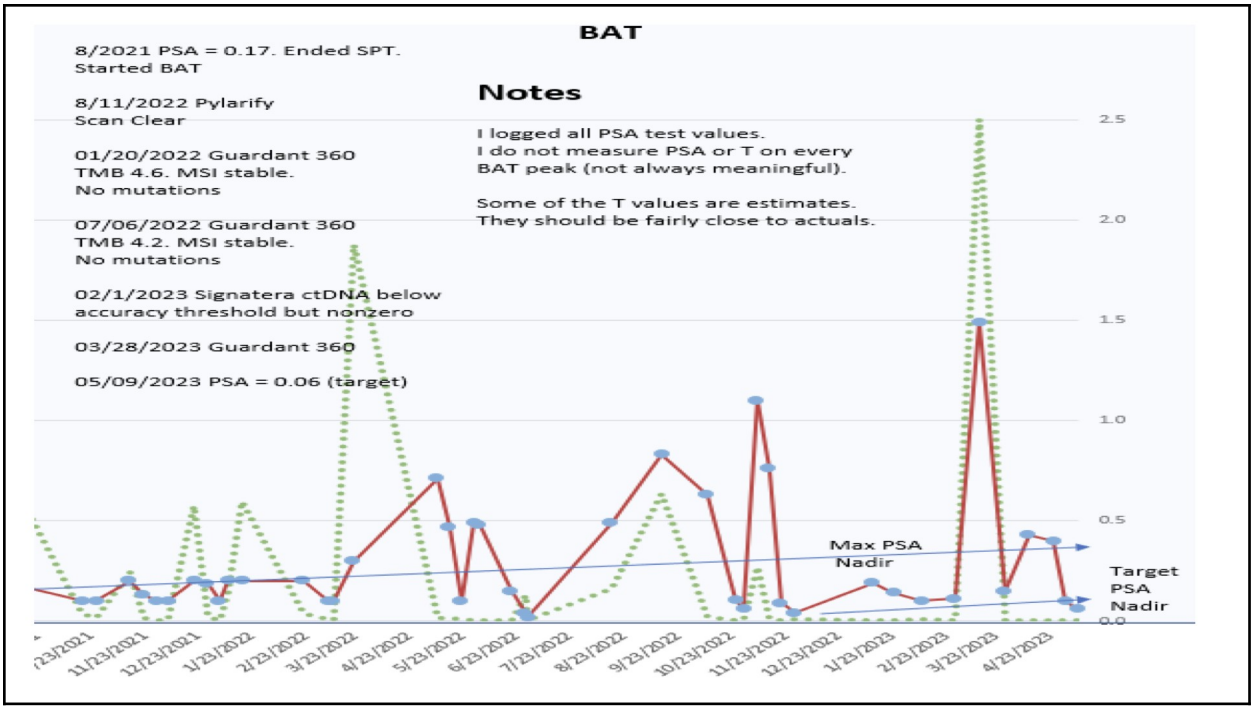

Here are my BAT results, if you can see that chart here is when I had RP (radical prostatectomy) about five years ago, then I did estrogens. For a month I used Casodex and Dutasteride. Then I used high testosterone constantly in this green area here, and then the blue area is BAT. You can see my PSAs are lower today than what they were a year and a half ago when I started (as of June 2023 they are a little higher than when I started BAT).

Clinical trials:

1. https://clinicaltrials.gov/ct2/show/NCT03734653
2. https://clinicaltrials.gov/ct2/show/NCT03554317
3. https://clinicaltrials.gov/ct2/show/NCT02090114
4. https://clinicaltrials.gov/ct2/show/NCT03516812
5. https://clinicaltrials.gov/ct2/show/NCT02286921
6. https://pubmed.ncbi.nlm.nih.gov/35938545/ https://clinicaltrials.gov/ct2/show/NCT01750398 (HSPC)
7. https://clinicaltrials.gov/ct2/show/NCT01084759
8. https://clinicaltrials.gov/ct2/show/NCT04424654
9. https://clinicaltrials.gov/ct2/show/NCT00586898
10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2738932/ (NCT00006044)
11. https://clinicaltrials.gov/ct2/show/NCT04558866
12. https://clinicaltrials.gov/ct2/show/NCT04704505

Not complete:

1. https://clinicaltrials.gov/ct2/show/NCT04363164
2. https://clinicaltrials.gov/ct2/show/NCT05081193
3. https://clinicaltrials.gov/ct2/show/NCT03522064
4. https://clinicaltrials.gov/ct2/show/NCT05011383

Study:

1. https://aacrjournals.org/clincancerres/article/12/24/7414/193013/Rapid-Androgen-Cycling-as-Treatment-for-Patients

Bipolar androgen therapy (BAT): A patient's guide – PMC https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9313844/
Dr. Sam Denmeade has volunteered to help MOs provide BAT to their patients. denmesa@jhmi.edu
I'll help however I can. smurtaw59@gmail.com

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Here's a list of clinical trials and Denmeade wanted to help anybody. I included his contact info, and also his Patients Guide to BAT and then my contact info there.

Summary Slide