“Starving Tumors with a Therapeutic Diet” (John Chant) [#36]

Brad Power
December 7, 2022

“The hypothesis is that you lower an amino acid, and that starves the tumor.” John Chant

Meeting Summary

Advanced cancer patients are looking for any boost they can get through lifestyle behaviors (e.g., exercise, meditation) or diet to complement their main medical treatments (e.g., drugs, radiation, surgery). Food can strengthen their defenses against their cancer (e.g., their immune system) or even possibly attack their cancer cells. Cancer cells are different from normal cells, and there is a search for ways to starve the cancer cells while supporting normal cells.

Filtricine is a biotech startup founded by researchers who came from Stanford to see if they could starve cancer cells with a restricted diet. They are developing a nutrient formulation which attempts to identify and exploit cancer cells’ metabolic vulnerabilities (the chemical processes that produce energy and basic materials needed for survival). Their diet eliminates some amino acids that cancer cells need but aren’t needed by normal cells.

How far along is the Filtricine product?

It’s very early days. Filtricine is recruiting patients for an observational trial where they look at how patients respond to their diet. They use each patient as a control by switching them on and off their treatment (a “crossover trial”) to see how they respond. They have tested about 20 patients so far. A few patients seem to have responded.

What are the ideal characteristics of a dietary product that would help cancer patients?

In the discussion which followed, patients shared their views on the ideal characteristics of a dietary product. It should…

- Taste good
- Be healthy
- Be taken for a short time, or intermittently
- Support, not replace treatment
- Be personalized (e.g., medical situation, vegan, other dietary preferences)
- Be easy to transition to
- Meet taste expectations (e.g., chicken noodle soup)
- Be supported by scientific evidence
- Be supported by treating physicians

For further information about Filtricine or to volunteer to try their diet, please contact John Chant at johnchant@filtricine.com.

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Meeting Notes

SUMMARY KEYWORDS

diet, patients, amino acids, cancer, people, food, psa, product, question, therapy, jimmy, oncologist, eat, data, tumor, study, lipids, prostate cancer, trial, nutrition

SPEAKERS

John Chant (62%), Brad Power (13%), Brian McCloskey (6%), Richard Anders (4%), Eric Hall (4%), Kevin Fordney (3%), Ken Anderson (2%), Stephanie Hall (2%), Jim Ward (2%), Jimmy Wang (1%)

Brad Power (0:04)

John Chant and Jimmy Wang are representing Filtricine. This is one in a series of meetings that we've focused on nutrition and diet and how it can impact cancer. In particular, down in the metabolic pathway, are there certain things that you can eat, or are there any angles on nutrition that could slow cancer progression? That's the focus of our conversation today. We had a previous session from a couple of patients' points of view on experiences they've had on using nutrition and supplements, and we're going to have a couple more as well. That sets the stage.

John Chant (0:58)

“Starving Tumors with a Therapeutic Diet” (John Chant) [#36]

CEO John Chant

Filtricine

Education/Academia (1985-2001)

UCSF
PhD, Genetics

Harvard University
Associate Professor
Biochemistry and Molecular Biology

Biotech/Pharma (2001-2007)

CuraGen
Head
Genomics Proteomics, Clinical Markers.

Genentech
Associate Director
Oncology, Genomics, Clinical Trial Research

CEO Positions (2008-present)

G1 Therapeutics. GTHX.
Founder and CEO
Oncology.
Peak market cap $2 billion

Gatekeeper Pharmaceuticals
Founder and CEO
Oncology
Successful exit: confidential

Alpha Eleven Therapeutics
Founder and CEO
Anticoagulant

Filtricine, 2000-Present
CEO
Treating cancer and metabolic diseases

UCSF University of California San Francisco

CuraGen Corporation · Genentech IN BUSINESS FOR LIFE · G1 THERAPEUTICS · GATEKEEPER pharmaceuticals · ALPHAELEVEN THERAPEUTICS

I've been in charge of Filtricine for about two years. My background is very heavily in therapeutics. I met Filtricine about four years ago. I was a friendly adviser and then a consultant. Then they asked me, based on my experience, to take over running the company.

The Logic of Our Approach

Filtricine

Is cancer a disease of metabolism?

Yes. Nobel Prize 1931.

Do cancer cells have different nutritional needs than healthy cells?

Yes. Cancer cells are growing uncontrollably. 95% of healthy cells are not growing.

Can cancer be treated by depletion of nutrients required by cancer and normal cells?

Yes. Asparaginase, which depletes the amino acid asparagine, is an approved FDA drug.

Can diet be used to deplete the nutrients required by cancer cells?

Yes. Reducing intake of amino acids reduces their level in the bloodstream.

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The whole idea of Filtricine is very simple. It's that cancer cells are different from normal cells, which we all agree. Cancer cells require nutrients, some nutrients in higher amounts than normal cells.

Corporate Profile

Filtricine

- Technology from Snyder Lab Stanford University School of Medicine
- Founded 2018
- Laboratory discovery to clinic in three years

- Novel and powerful approach to cancer treatment and patient care
- Product 1: Cancer treatment
- Prostate cancer trial completed at Stanford: positive results
- Cancer product: commercial launch 2023-2024

- Product 2: Dietary treatment for NASH/NAFLD
- Product 3: Cholesterol and lipid lowering diet
- Launches in 2024 or earlier (cholesterol)

- 2018-2021: Raised $7.5M – Seed I and II
- Series A raise: TBD for 2023-2024

Stanford University

PG 3

That's well established and was better established by Jimmy Wang and Xiyan Li when they were at Stanford University in Mike Snyder's lab.

Overview

Filtricine

Filtricine's Food as Medicine Approach

The Science

- Cancer cells are different than normal cells
- Cancer cells have heightened requirements for certain nutrients: Non-Essential Amino Acids (NEAA)
- Cancer cells are deficient and acquire NEAA from the bloodstream
- Normal cells synthesize NEAA internally

How to Use: Tality Meal Replacement Plan

- Can be used as single agent
- Can be used in combination
- Complete or partial meal replacement

The Mechanism: Targeted Nutrient Deprivation (TND)

- Depletes the NEAA that feed the cancer
- We do this with foods deficient in the target NEAA
- Food as medicine

Safety

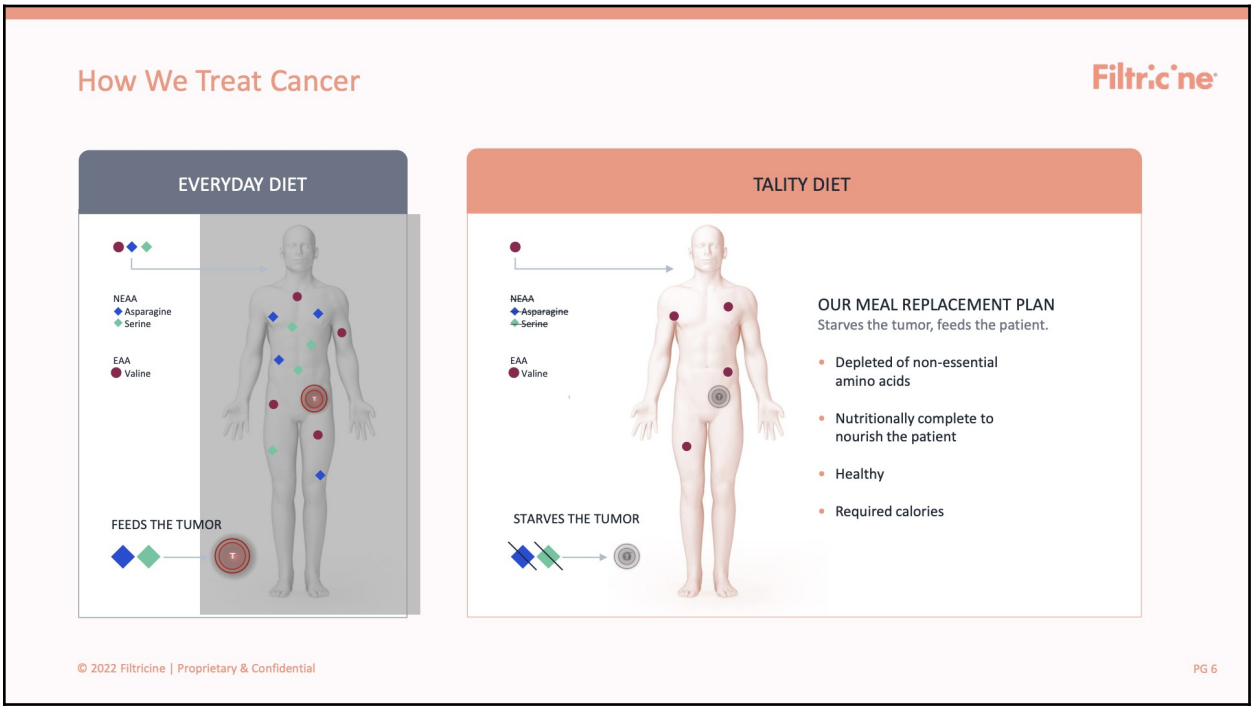
- Diet is complete and healthy
- Drug free = very safe
- Animal and human data confirms safety

PG 5

First, cancer cells are altered. Second, they require certain nutrients more than our normal cells. And then finally, it turns out a very easy way to reduce levels of those nutrients that cancer cells require is by a formulated diet. The scheme of our science, and our clinical approach, is to feed cancer patients a formulated diet, lacking certain amino acids. These are non-essential amino acids. They're amino acids that you don't need in your diet because your normal cells can make them, but cancer cells have a heightened requirement for them. It's very simple. We feed patients, and we're doing clinical trials and volunteer studies right now, on a diet that lacks these non-essential amino acids.

We're looking at the level and velocity of PSA in prostate cancer patients now. I'll show you a couple slides of data that show encouraging results. We think we're seeing an early signal of slowing the rise of PSA. It's early days. That's our first dietary formula. We've improved the formula a lot through experiments by Xiyan and Jimmy. We think that we can improve the results to a great degree.

When I met the company a few years ago and heard about food and cancer as treatment, I'll be honest, I was a little skeptical, with my therapeutics and a pretty scientific background. But then I thought that the foundations of logic, which I mentioned, are completely correct. If you want to be dismissive of this idea, one would have to conclude that what one eats has nothing to do with what goes on in your body, and what goes on in cancer cells. It's a nutrient limiting, lowering diet. Again, these are nutrients your body does not need, because they can make them in your normal cells. It's very akin to diabetes, where we know mild diabetes to moderate diabetes can be managed by sugar intake and the diet they have.



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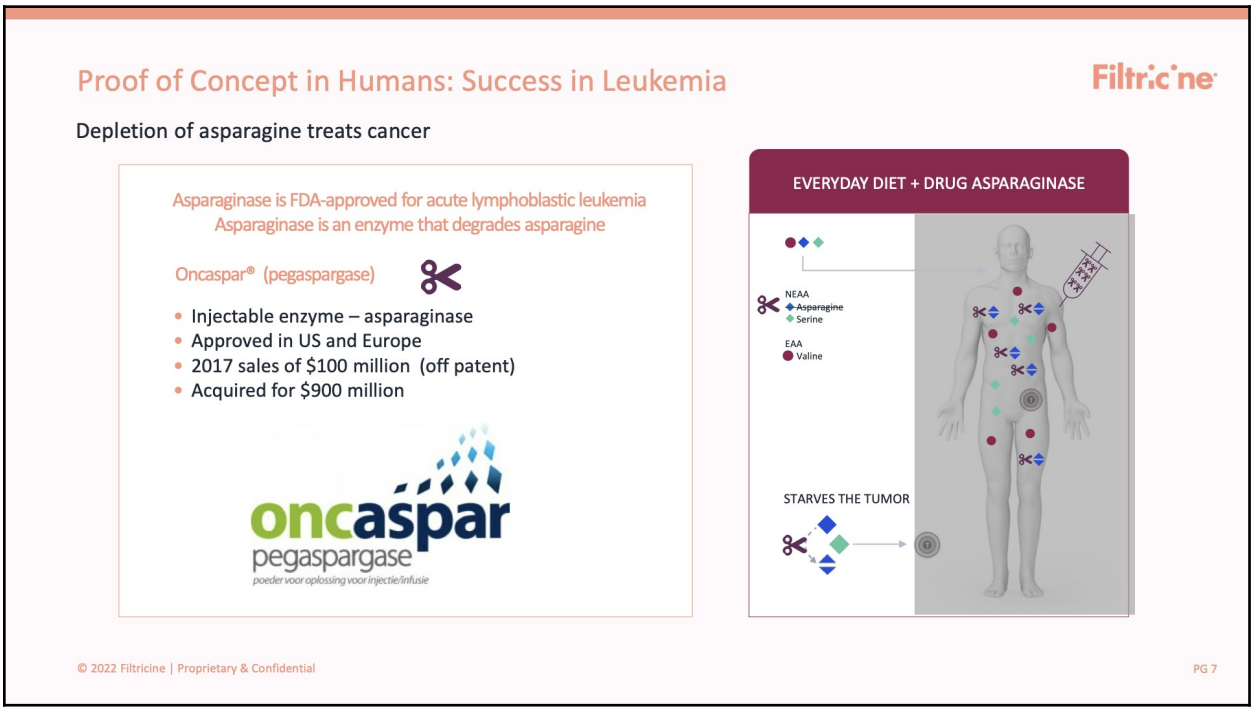
Here's a schematic of the basic scheme. Your diet normally requires about 20 amino acids for making proteins, and there are other supports. The character on the left on an everyday diet receives a full diet of these amino acids. There are 11 non-essential amino acids, and 9 essential, so about 20 amino acids total in your diet, and some other more minor ones. He is receiving all these and his tumor in this case is fed by asparagine and serine. They're feeding the tumor, and the tumor is growing. But if you make a diet that has asparagine and serine completely removed, then the tumor is starved. I won't go through all the data.
[Note 20 amino acids; I show three for simplicity]

This came out of Mike Snyder's Lab at Stanford, and the great work of Jimmy Wang and Xiyan Li. Jimmy's here. I didn't really introduce Jimmy. Jimmy is a medical doctor, who is our CTO of the company and has worked in the drug development field and cancer field for a long time and the metabolism field for a long time.



Is there proof of the concept of reducing amino acid levels in your blood to treat a tumor? Based on my background in pharmacology and drug development, a lot of companies have great ideas, but the question is, does it work in people? There's a proof of concept here that really reassured me. In a type of leukemia, acute lymphoblastic leukemia, there's already a therapy that gets rid of one of the amino acids, asparagine, by injecting an enzyme called asparaginase. (Asparaginase is used to treat acute lymphoblastic leukemia and is being studied in the treatment of some other types of cancer. It is an enzyme taken from the bacterium Escherichia coli. It breaks down the amino acid asparagine and may block the growth of tumor cells that need asparagine to grow.) There's one example in cancer. It's a recurring theme. It would be unreasonable to believe that this one tumor requires an amino acid, and no other tumor in the

vast spectrum of different types of cancers would require amino acids. This was very reassuring that the general scheme could work.

What's our product? We have a menu of formulated foods that contain all the nutrients you need. It has about 24 or more components. Though the names may be different, all these foods have the same formula, in that they're lacking non-essential amino acids. This is what patients receive. One reaction we've had is that if this works you're going to have to eat this food for the rest of your life to get the therapeutic benefit. A couple of things. It is quite clear that intermittent dosing, a period on and a period off, will probably work. And we have very strong evidence to show that eating this food as part of your diet, and not all of your diet, with normal food, is very likely to work.

This is early days. The company was started in 2018. We've got the clinic in just a few years. One thing I've learned in the pharma industry is that you can do a lot of animal studies and what have you, but you want to get to humans as rapidly as possible to see if you have a signal, is the right way to do things. This is preclinical data.

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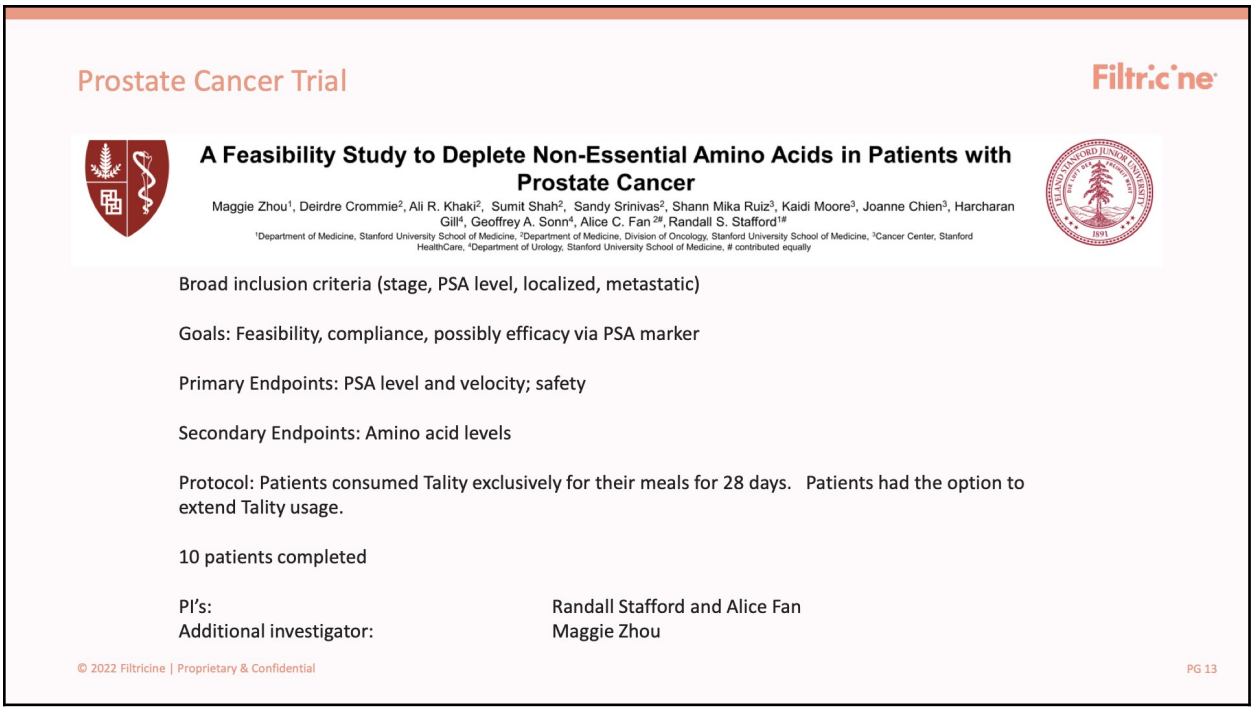


Prostate Cancer Trial

Filtricine

A Feasibility Study to Deplete Non-Essential Amino Acids in Patients with Prostate Cancer

Maggie Zhou[1], Deirdre Crommie[2], Ali R. Khaki[2], Sumit Shah[2], Sandy Srinivas[2], Shann Mika Ruiz[3], Kaidi Moore[3], Joanne Chien[3], Harcharan Gill[4], Geoffrey A. Sonn[4], Alice C. Fan[2#], Randall S. Stafford[1#]
[1]Department of Medicine, Stanford University School of Medicine, [2]Department of Medicine, Division of Oncology, Stanford University School of Medicine, [3]Cancer Center, Stanford HealthCare, [4]Department of Urology, Stanford University School of Medicine, # contributed equally

Broad inclusion criteria (stage, PSA level, localized, metastatic)

Goals: Feasibility, compliance, possibly efficacy via PSA marker

Primary Endpoints: PSA level and velocity; safety

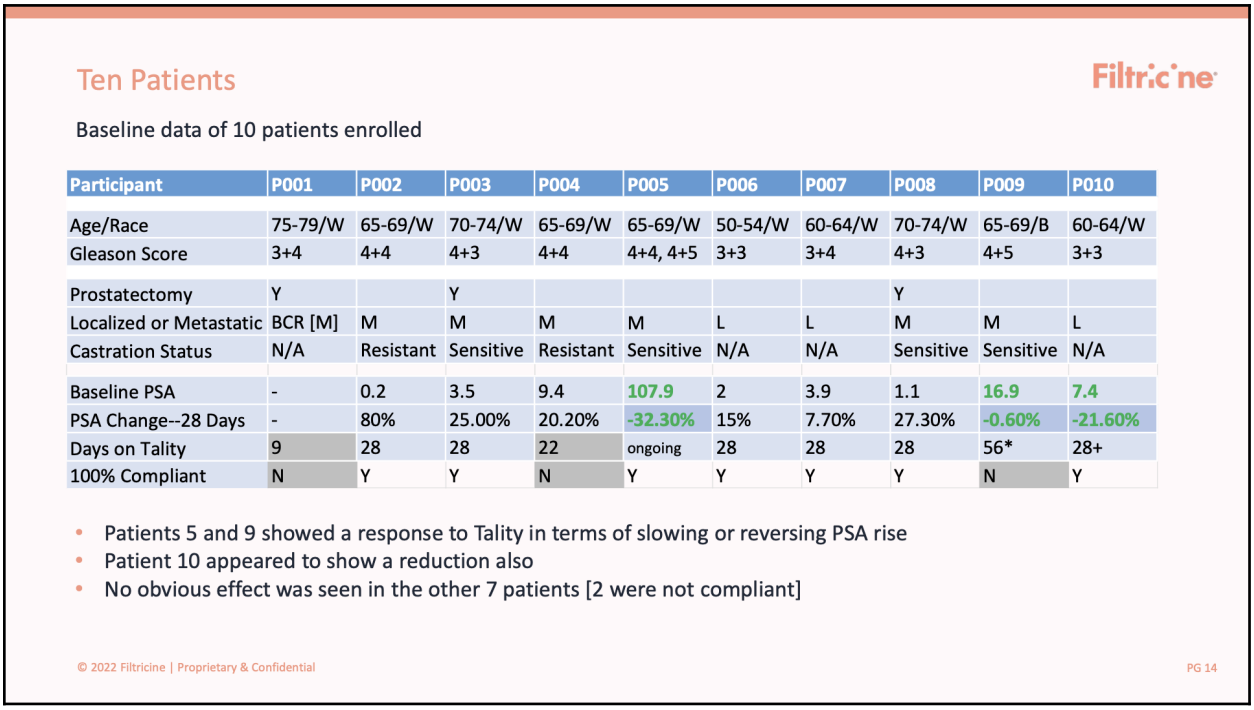
Secondary Endpoints: Amino acid levels

Protocol: Patients consumed Tality exclusively for their meals for 28 days. Patients had the option to extend Tality usage.

10 patients completed

PI’s: Randall Stafford and Alice Fan
Additional investigator: Maggie Zhou

Here's a study we performed at Stanford University with Alice Fan and Randy Stafford as PIs (principal investigators).



Ten Patients

Filtricine

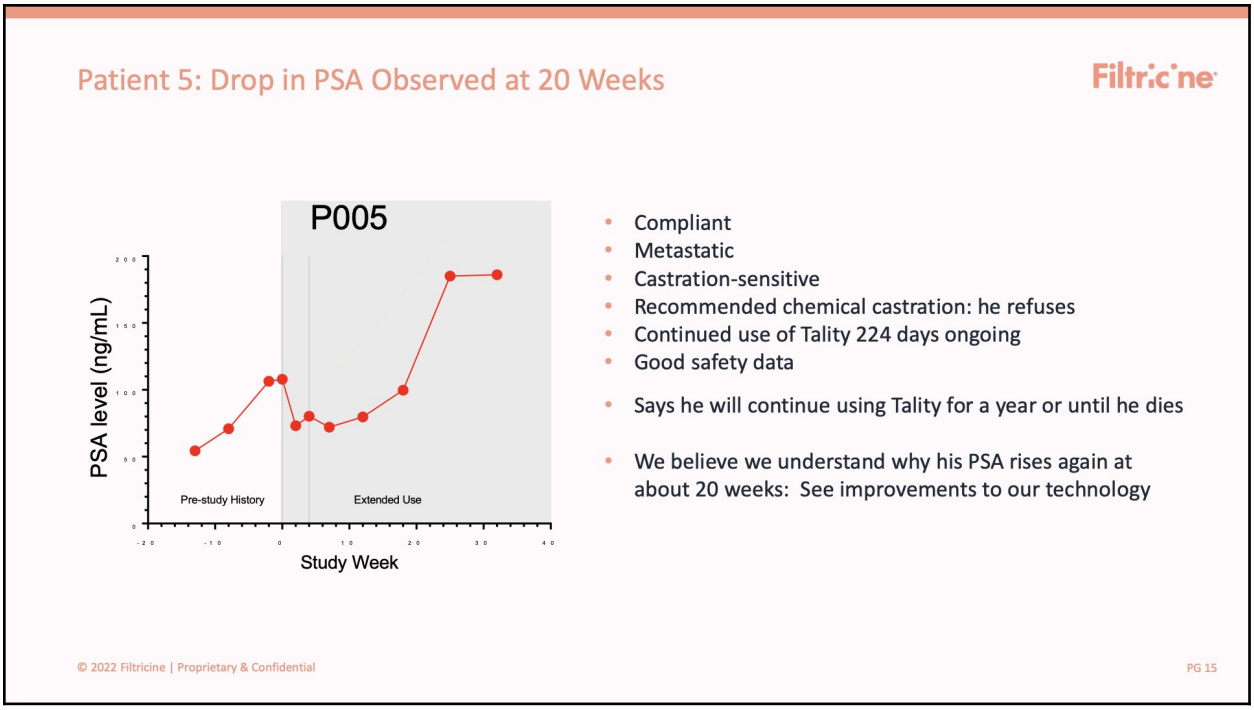
Baseline data of 10 patients enrolled

Participant	P001	P002	P003	P004	P005	P006	P007	P008	P009	P010
Age/Race	75-79/W	65-69/W	70-74/W	65-69/W	65-69/W	50-54/W	60-64/W	70-74/W	65-69/B	60-64/W
Gleason Score	3+4	4+4	4+3	4+4	4+4, 4+5	3+3	3+4	4+3	4+5	3+3
Prostatectomy	Y		Y					Y		
Localized or Metastatic	BCR [M]	M	M	M	M	L	L	M	M	L
Castration Status	N/A	Resistant	Sensitive	Resistant	Sensitive	N/A	N/A	Sensitive	Sensitive	N/A
Baseline PSA	-	0.2	3.5	9.4	107.9	2	3.9	1.1	16.9	7.4
PSA Change--28 Days	-	80%	25.00%	20.20%	-32.30%	15%	7.70%	27.30%	-0.60%	-21.60%
Days on Tality	9	28	28	22	ongoing	28	28	28	56*	28+
100% Compliant	N	Y	Y	N	Y	Y	Y	Y	N	Y

- Patients 5 and 9 showed a response to Tality in terms of slowing or reversing PSA rise
- Patient 10 appeared to show a reduction also
- No obvious effect was seen in the other 7 patients [2 were not compliant]

It's very simple. We took all prostate cancer patients, only ten in this case, and we asked them to go on our diet for four weeks. Then we measured their PSA. My father had prostate cancer, and then had a prostatectomy. I know more about PSA than I would have known otherwise, just

as a scientist. PSA is very critical to monitoring progress of your tumor, especially in more advanced stages, and in guiding therapeutic choices. Of the ten patients, some had a prostatectomy. Some were metastatic. Some were localized. We saw that two or three patients out of the ten in our first attempt at feeding this diet to patients seem to have a diminution of PSA or a slowing of PSA rise. I like to be very cautious about scientific data. We asked Alice Fan, who was the PI and a full time oncologist, whether there was any explanation for this other than our diet having the effect. The way we ran the trial was on their regular diet then on our diet and then back on their regular diet. Whatever you want to call it, “crossover”, or “ABA”.



Here's one patient, patient five. He's continued on the diet much longer than was required at Stanford University. We show here his rise in PSA. On the left hand side is his rise prior to the study, and then the gray period is when he's on our diet.

John Chant (10:53)

To personalize this a little bit, he was very compliant. He was metastatic castration sensitive, but for his own personal reasons he chose not to. He wanted to try our diet. We did not see a cure for his cancer. But during the 20 weeks, the diet, as measured by his PSA, managed to slow his PSA rise and cause a drop in PSA. Then subsequently, it eventually did go up. This is as, unfortunately, we know, quite common with drugs also. We think we understand why it went up. This is our very first study, putting this diet into patients again after just a few years. We consider this very encouraging. We're very excited and proud of this.

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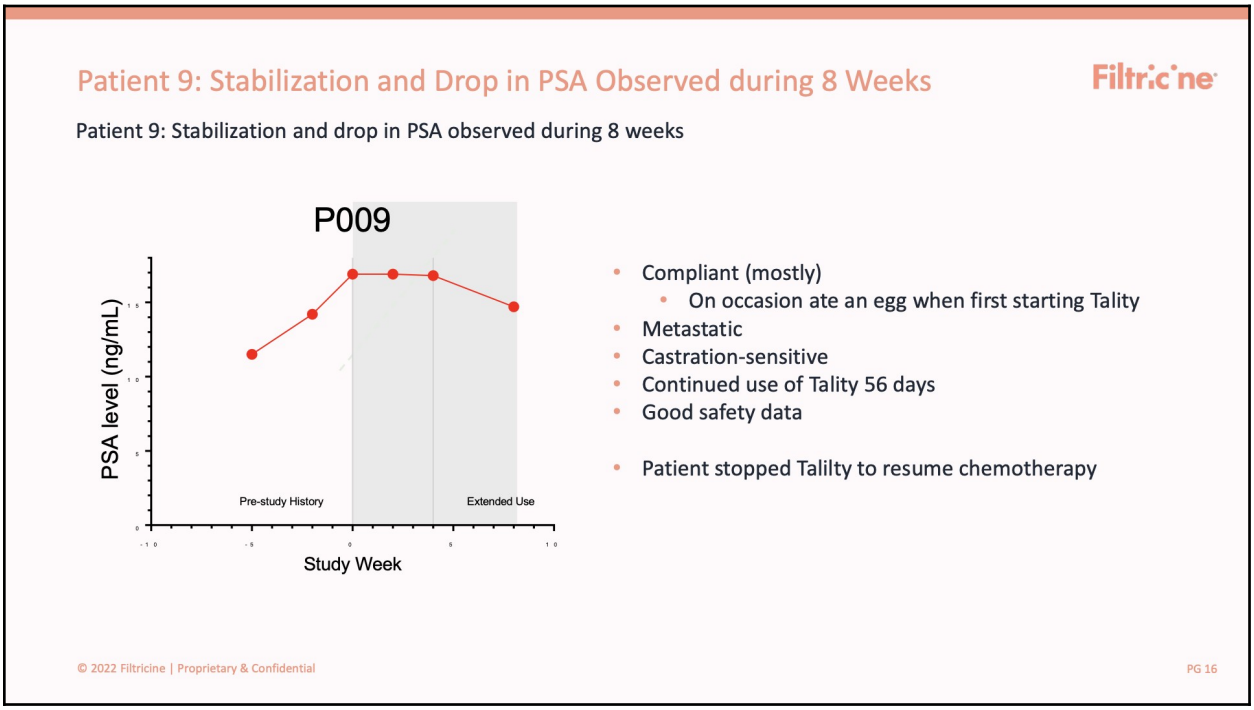
[This patient eventually went on to treatment with Lutentium-177 PSMA; his response is very good so far. He credited out diet with slowing his PSA rise and giving him more time to find this option and to avoid hormone-reduction therapy.]



Here's patient nine. Going into the study, his PSA was rising, so called “velocity”. As soon as he was put on our diet, which we call Tality, his PSA rise stopped, and then his PSA levels tended to go down. This all comes from Jimmy and Xiyan in Mike Snyder's Lab at Stanford. We're caught up in the details day-to-day running this and doing these trials. This is the first time, to my knowledge, where someone has shown that depleting nutrients in a diet can be used for treating cancer. There is a little bit of data there about intermittent fasting and starvation. But that's sort of a nonspecific effect. Here, we've taken a very precise effect approach of depleting amino acids that we think are important for the tumor. We believe, and our oncologist believes, at Stanford, that we've seen an effect, at least in some patients. There's a lot of additional information I can provide. That's our high level approach.

In terms of the company, we're planning to commercialize this in 2023 or 2024. Because this is a medical food, it does not require FDA approval and six-year studies.

Our diet is 100% healthy because we have formulated it based on FDA guidelines. In addition to having what appears to be a therapeutic benefit, in many cases patients felt benefits to their quality of life in terms of their strength and their robustness. They reported getting rid of problems like sleeplessness, or brain fog, things that can happen when one's under an intense therapeutic regimen.

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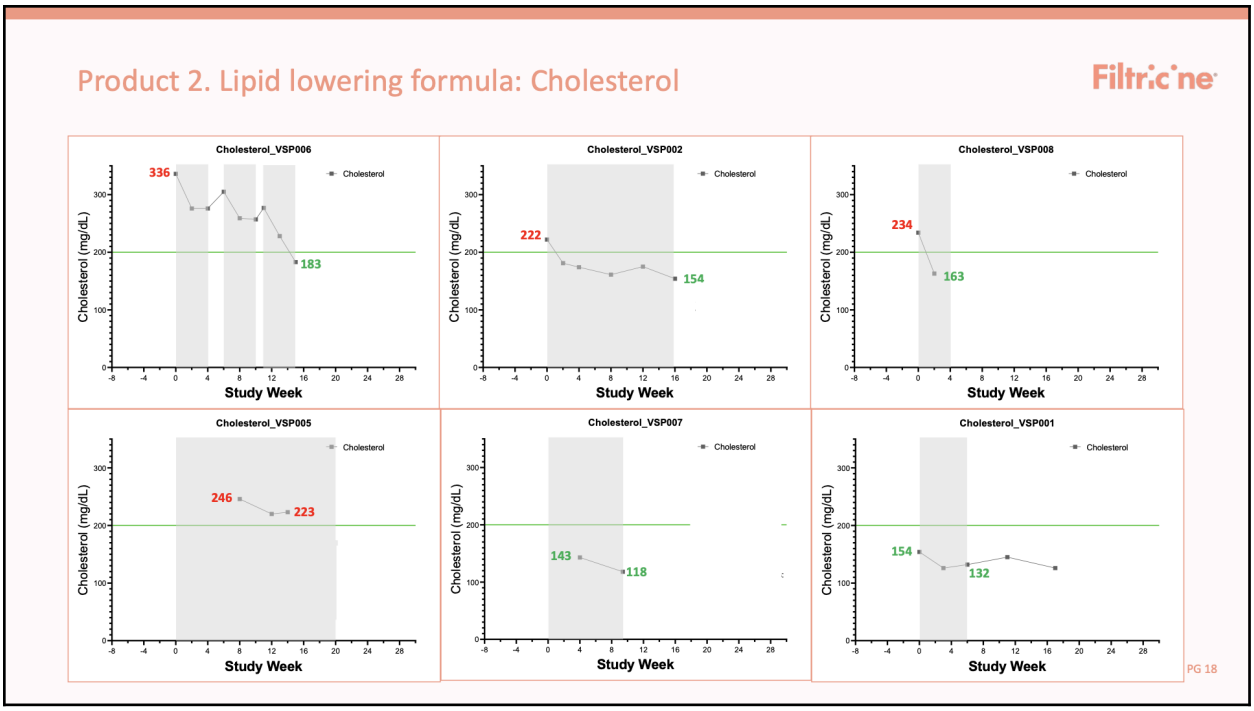

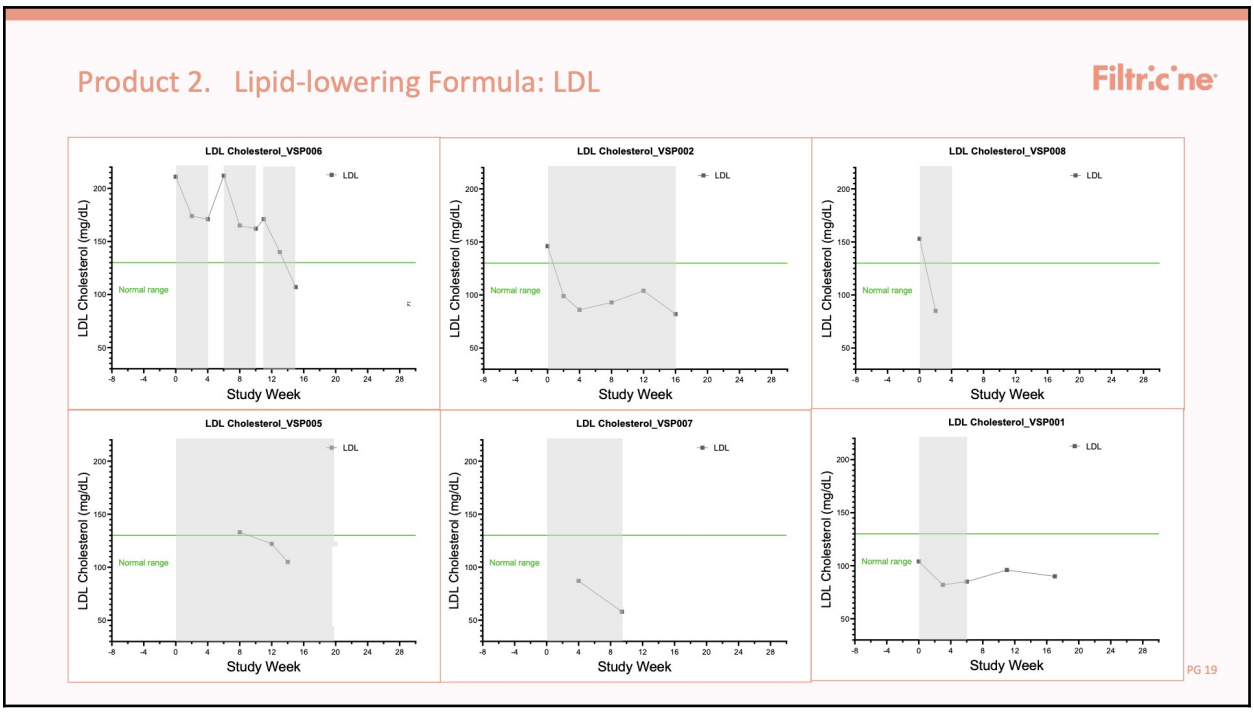

We also have looked at lipid lowering, which is a concern for older people. When we provide a special diet depleted of nutrients, we see a very strong lowering of lipids in patients that have high levels of cholesterol, or LDL. We've come upon a therapeutic approach, but accomplished by diet. Since this diet is just food depleted of certain nutrients, it really has no side effect profile, or an extremely mild side effect profile, which contrasts to the case of a lot of drugs for cancer, especially, and even drugs for things like lowering cholesterol.

We have a volunteer program. Anyone who might be interested, with any type of cancer, we're happy to let them test the food if they would like.

Stephanie Hall (16:30)

What is the type of protein used in most of the products?

John Chant (16:41)

The only way you can create a product that I know of that's depleted of multiple amino acids is you have to do it using monomeric amino acids. There are no polypeptides or intact protein.

Stephanie Hall (16:55)

When you talk about the lipid lowering benefit of it, I’m not an expert, but my understanding is there's some research showing for prostate cancer in particular, that the use of statins can prolong the time to castrate resistant for men with prostate cancer. That's because it is approaching it from a metabolic pathway and blocking that uptake, reducing lipids. Do you use berberine, which is a kind of a natural statin, or is it just that taking out these amino acids has the result of lowering the lipids? (Berberine is an alkaloid found in the barks, leaves, twigs, rhizomes, roots, and/or stems of various plants, such as the barberry, Oregon grape, and tree turmeric. Berberine is a dietary supplement that has been shown to lower blood sugar, cause weight loss, and improve heart health. Traditionally, berberine has been used as an antimicrobial, antiprotozoal, and antidiarrheal agent in Ayurvedic medicine and traditional Chinese medicine.)

John Chant (17:36)

It is taking out the amino acids. We've not done anything further or special. We haven't really worked on the lipid profile of the product. This was a little bit unexpected. They must have had some reason to do this. I give them credit.

Stephanie Hall (17:57)

I was just wondering if it had vitamins and minerals, including the vitamin berberine. Can it lower lipids?

John Chant (18:06)

I'll look at berberine.
It contains all the standard vitamins and minerals, but no, not that one.

Stephanie Hall (18:22):

That's a great added benefit that it does lower lipids, because with the studies that I read, men with prostate cancer that didn't have high cholesterol markers benefited from having the statins and the lipid profiles reduced. It's a great added benefit.

John Chant (18:42)

We'll look at this right away.

Brian McCloskey (18:55)

What were the different treatments that the patients were on? Did they have to take a break? And if they did take a break, how long was the washout period for each of the different treatments?

John Chant (19:18)

Since the product doesn't have side effects, we think we can use it almost anywhere, but we ran the trial as single agents so we could intelligently analyze what was going on. For the patient who didn't want to take hormone reduction therapy, I'm not sure if he had therapy previously. He was a science contrarian. He was not on therapy at any time. The other one went off the diet even though his PSA stabilized. He went off the diet because his oncologist suggested that he take chemotherapy, but then that was after. We were careful to have a washout of 30 or 60 days at the very least.

Jimmy Wang (20:26)

At Stanford, all the patients had to be stable. If they had any previous change in their therapy, they had to have a 90 day washout period.

John Chant (20:49)

We were allowing them to take the diet on top of stable therapy. In the case of these two patients, it was not that way. I don't think that any of our patients were on any sort of significant anti-cancer therapy when they took the diet and again, the washout. They didn't have any of that time. A requirement was the washout had to be 90 days.

Brad Power (21:44)

This sounds like you're doing an observational trial. People are trying it, and you try to see if there's an effect on their PSA (for the prostate cancer patients). The gold standard in medicine generally is the randomized clinical trial, where you randomly give some people a placebo and give some other people the treatment. Where are you in building the evidence base? Our patients have very conservative medical advisors. So they would be looking for something

perhaps more substantial than an observational trial. They might say, “Well, that could have been something else, not the stuff you're taking.” For example, as a joke, it could be because this stuff tastes so bad that I stopped eating. Intermittent fasting. There could be other factors that a skeptic would raise. How would you answer that kind of challenge on evidence?

John Chant (23:30)

We're going to bring this to market as medical food. We're not going to do a randomized controlled trial. My strong view is that a longitudinal study, if done with sufficient numbers and carefully, is sufficient. Let me step back a little bit. One way of doing a trial, rather than the randomized control trial, is a crossover trial, where you have a patient for any therapy. If they're off the therapy, they go on the therapy, and then they go off, or another patient has an extended period being off and then goes on, and seeing if there's a difference when they go on the therapy. That's one way of doing a trial. There's a lot of power to having the patient as their own control. PSA can range from 0.2 to 1000 or 2000. If there's one thing we know about cancer, it's that it's very heterogeneous. That's one reason, among many, that we like to have the patient as their own control.

In terms of evidence for physicians, response from physicians has generally been pretty positive. We have volunteers. We have their patients who were asked to be on the trial, who didn't go on the trial. For whatever reason they didn't choose the idea. Some people are really looking for this sort of thing rather than drug treatments, some of which are very harsh. The attitude we've had from some cancer patients is that there are no side effects, so there's nothing to lose. Physicians have been very accepting.

John Chant (25:39)

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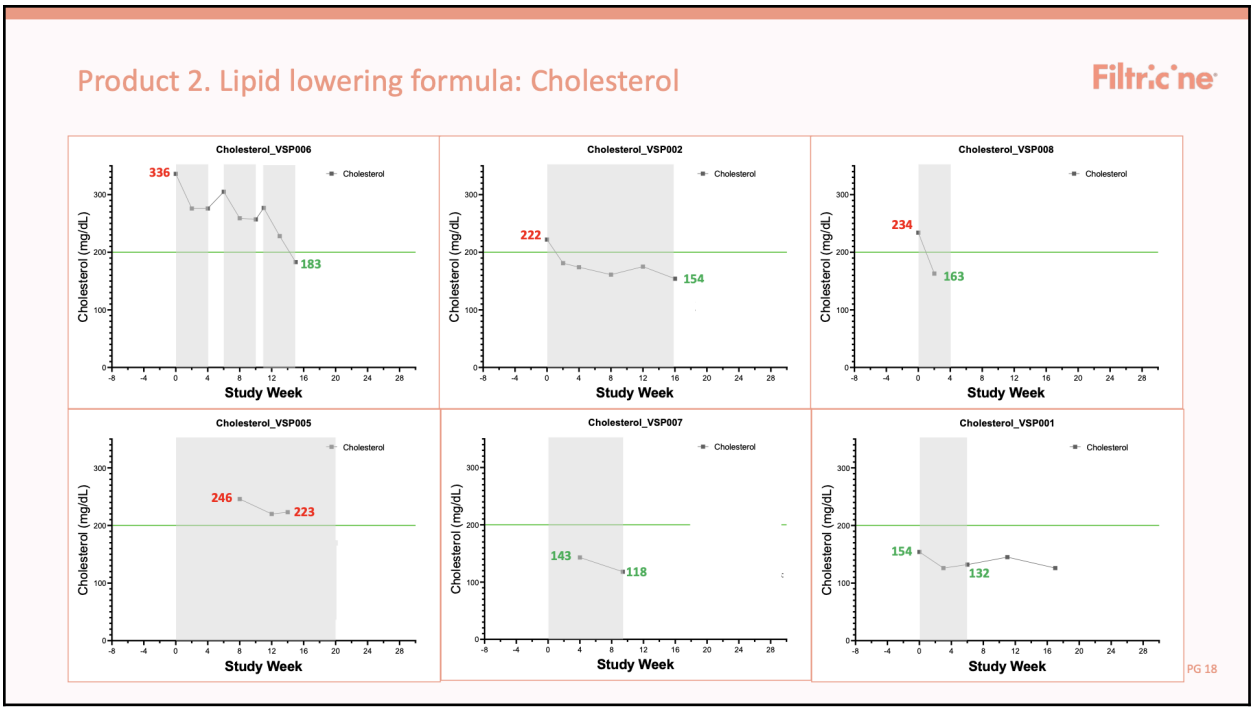

This slide is speaking to crossover trials, which are on again, off again, on-off trials.

I'm not showing the prostate data. Here are two patients. It could be due to something else. I've been assigned this for a long time. That's for sure.

Look in the upper left at one of the volunteer patients. We looked at his cholesterol. He went on to this cholesterol lowering diet, periods marked by gray, and then he went off, then on, then off. This was true for his LDL and other lipid markers as well. Even though this is not a randomly controlled trial, it's hard to explain this triple drop completely coincident with when he was on the food by any other explanation. I agree, we need higher numbers. We're running further trials on prostate cancer and further trials on other types of cancer to get the numbers up and get additional data. I'm steadfast against running a thousand-person random control trial.

Brad Power (27:16)

How many patients roughly do you have data for?

John Chant (27:22)

About 20.

There is an example of one company I won't name in the metabolic space, trying to block an amino acid by pharmacological means that spent $100 million in seven years and failed. One mission of a startup is to do things. We could ask for $50 million or $100 million to do a

randomized controlled trial, but another mission of a startup is to try to do things as efficiently and effectively as possible. That's what we're trying to do.

Jim Ward (28:21):

You've highlighted one of the effects of your diets is lowering lipids. I say this as a guy who takes statins off label because I've heard of that benefit. But what I don't know, and I hope you can maybe shed some light on, is the physiological or biological connection believed to be between lipids and cancer cell growth, in particular for prostate cancer cell growth?

John Chant (28:54)

I honestly don't know. Jimmy and I will look into it and get back to you with an answer. It's intriguing. In the formula, we have the ability to modify lipids. Sorry I can't give a more satisfying answer.

Jim Ward (29:21)

If someone were to do this diet, what is the typical daily caloric intake on this diet and protein intake? I'm one of those guys that is not battling to keep weight off. I'm battling to keep weight on, and I'm not on hormone therapy. I'm trying to take advantage of having regained testosterone to build muscle and keep my weight, but I worry a little bit that if I'm eating stuff too low in protein/calories, then I'm just going to be on my wife's diet. It's very effective for her, but it would probably tend to drive me crazy.

John Chant (30:03)

The diet is calorically complete. We have had people ask for higher levels of calories, such as athletes, even triathletes. It can be modified in any way. Recently we've been exploring the tolerance of adding regular food to this. You have to be primarily on this diet, but you can be on three weeks, one week off, or something like that. We're not sure of the possible permutations. You could have two meals of our product and one meal of regular food. We're still exploring that.

We have a marker for how effectively the diet is working. A certain amino acid in the blood is what we would call a pharmacodynamic marker, which reliably shows how effectively the diet is working for you in changing your metabolism. Then the second question is, “How much is changing the metabolism affecting the tumor?” Because tumors are heterogeneous. We could put you on a diet by whatever regimen you want, and then look at the pharmacodynamic marker to determine how much it's affecting your metabolism. We have a good answer there.

Since it's early days, we take all comers. If you want to do 50/50, we'd prefer you do about 80/20 of our diet versus regular diet, but since we don't understand everything entirely, we're open to all volunteers or all people who are interested.

Eric Hall (32:04)

I'm very big on lifestyle and diet things while trying to support my medical treatments. Since being diagnosed, I have switched to being vegan along with gluten free. Do you have products that work for me, with my kind of specialized diet, with no animal products?

John Chant (32:38)

Our diet has no animal products in it. On a vegan diet, you're probably challenged a little bit to keep your protein levels up. Our diet has the normal levels that you would get from eating meat, or on a standard diet. This is, for better or worse, a completely synthetic diet.

Eric Hall (33:08)

What does it use for protein? Is it like hemp seeds, pea protein, spinach, or anything like that?

John Chant (33:15)

No, it's amino acids. It's pure.

Eric Hall (33:20)

Do you have different foods for different cancer types, or maybe even personalized for different different people based on their genetic makeup or something else?

John Chant (33:36)

The answer is we don't. We've created a diet. I hesitate to say the exact number, which is a trade secret, but our diet is depleted of almost all the 11 non-essential amino acids. It takes a broad swath, knocking out amino acids that your body doesn't need. Our approach has been to use this for all cancers because it does not have side effects. That's a big concern. Rather than personalizing it to certain types of cancers, because it's safe, we can try this on every cancer in the future. It may be more personalized, but that's a lot of work.

Eric Hall (34:31)

I saw some of your flavors were like chocolate and other things. Does it have sugars or sweeteners in it to get those flavors? Sugar is a very non-anti-cancer ingredient for a lot of anti-cancer diets.

John Chant (34:55)

There's not a lot of sugar in it. There's a whole field of artificial flavoring. We have a terrific food scientist named Mike who's not here today. We've invested a lot into developing the foods. It's embarrassing to say, but it really is fake food to eat.

Richard Anders (35:30)

I've heard about your work for a while, so it's really interesting to see the presentation.

To confirm, it's really a constructed food, not based on anything like, say, vegetables, that some would think of as food, and you put together a flavor profile by designing combinations of allowed amino acids? That's the base product?

On a side note, do you have any use cases or success stories when the FDA-approved asparaginase product works particularly well? Has that been studied?

John Chant (36:14)

Asparaginase is used in certain types of leukemia, ALL. It was approved in the 1970s. It was found by accident. Asparaginase is used in combination with chemotherapy, and it is used in pediatric patients. Adult patients don't react well to it. In pediatric patients it is generally curative, as often is the case with, thankfully, pediatric cancers. It has been looked at in breast cancer. And there are some encouraging data, but not enough positive data to get it routinely used there. I know people are looking at other cancers. So far it has been nothing too positive.

Richard Anders (37:23)

The reason I was asking about asparaginase and the 11 non-essential amino acid hypothesis is that possibly there could be biomarkers, which would indicate constitutive dependency on some of those amino acids. Asparagine is probably one of those amino acids, and the approved asparaginase drug is depleting it. So that product doesn’t work on 11 acids, it works on one. Success stories for that one would be useful. Your data is clearly mixed. Presumably, it works sometimes, and it doesn't work sometimes, so this needs to be figured out better, or maybe the product needs to be honed? Or maybe there are certain cancers for which it would work better, and certain ones for which it wouldn’t work. I'm wondering, is there any set of biomarkers or any kind of exploration you've done to try to figure out which people would have cancers that are dependent on this pathway, and which are not?

John Chant (38:33)

We have published, and we've done cell culture studies, which again, I'm cautious about interpreting directly to patients. From cell culture studies you can see, at least for the number of cell lines we use, that the different types of cancer have different dependencies. I was in charge of biomarkers many years ago, and unfortunately to develop biomarkers in humans requires clinical data, so that you can decide what might be a biomarker in vitro. But to really validate it,

you need to do human studies, which is almost the same as what we're doing. It's interesting in animals. We depleted the same number of animals, and I didn't show the data, but the data is terrific. But a lot of companies have terrific data in mice. And that's why we wanted to get to humans quickly. You can do the experiment by adding back certain amino acids or changing the blend. That's on our agenda. That's the best we can do at the moment.

Richard Anders (39:34)

The difficulty with cell lines is that you pick your cell line for whatever reasons, and it can be easy to introduce a bias towards cell lines for which this works, even if those are quite unusual, and those are the cell lines that become used in the experiments. Of course, if it worked in all the cell lines you tested, that would be a very positive signal.

John Chant (39:56)

As a scientist, I would worry if it worked everywhere because that would suggest that there's not a specific mechanism.

Richard Anders (40:07)

It would be really interesting to do a PDX mouse study. I don't know how long this study would take. But if a patient was really interested and really wanted to test your product against their cancer, they could pay for a PDX.

John Chant (40:21)

Yes, they could. There are many companies that do in vitro testing of cells.

For any cancer therapy, sadly, I don't think you'd expect it to work on every patient. Because it’s a very heterogeneous disease.

Brian McCloskey (40:47)

I want to provide some color commentary on the taste of the food. About a year ago, I was able to take part in a little trial. One of the things that I had the biggest challenge with was the taste. I have a bit of a marketing background. I can take you through a scale on some of the products. This is just my take.

John Chant (41:24)

Let me say a couple things. Different patients obviously have different experiences. One challenge, other than taste, is transition to the diet. Patients have a tough time giving up regular food, and then once they get going, they feel a little better about it.

The other thing – maybe my palate is not as well developed – I ate all the food, although not for a month. I thought, “It's not like your favorite restaurant,” but I thought it was okay.

Brian McCloskey (42:00)

This is a data point of one. There were 13 different products that I had at the time.

	Category	Item	Tasting Notes	Recommend to a Friend (1-Not at all; 2-Maybe; 3 Definitely Recommend)	Category Average
1	Shake	Orange cream shake	This works. Not too sweet. Pleasing orange flavor.	3	
2	Shake	Mixed berry shake	Good berry flavor, pretty sweet, didn't dissolve completely	1	
3	Shake	Lemon shake	Chalky, too sweet	1	1.67
4	Soup	Ginger honey soup	Some ginger taste and maybe honey but a blind taste test would probably make it hard to pinpoint those flavors	2	
5	Soup	Beet borscht soup	Light pink color consistent with borscht. Flavor is good. Nice spice but a bitter aftertaste	1	
6	Soup	Roasted "chicken" soup	A bit bitter. Color not close to chicken soup. Doesn't really taste like chicken	2	
7	Soup	Santa fe style soup	Funky flavor; spice was OK but generally not pleasing; daughter said the color resembled vomit	1	
8	Soup	Tuscan veggie soup	Not bad. Taste the bean flavor but slightly bitter aftertaste.	2	
9	Soup	Corn bacon chowder soup	A bit of smoky flavor but bitter	1	1.50
10	Bar	Chocolate mocha chip bar	Good chocolate taste; similar to other bars on the market for taste	3	
11	Bar	Coconut date bar	Great date and coconut flavor.	3	
12	Bar	Roasted veggie bar	Unusually spicy for a food bar. Bitter. Not good	1	
13	Bar	Savory peanut bar	Great peanut flavor	3	2.5

—

Brian McCloskey’s Summary Comments

Bars:
I believe the bars were the best products as a category with the exception of the roasted veggie bar. 3 of the 4 "Definitely Recommend" came from this category.
Shakes:
2 of the 3 I would Definitely not Recommend. In general, they were far too sweet.
Soups:
With an average rating of 1.5 across 6 items, this category generally leaned unfavorably. There were no "Definitely Recommend" products. Several products had a bitter flavor.

[Note added by John Chant: We are very aware that texture is important in diet. We have expended some effort in adding solids to the diet. For example, konjac noodles, well known in diet circles, can be used with soups]
—

Brian McCloskey

So it looks like your menu has expanded. There were three different categories: shakes, soups and bars, and then I listed each of the different items, what my tasting notes were, and then I used, “Would you recommend this to a friend?” One is “definitely”, two is “maybe”, and three is “definitely would recommend”. You can see here for the shakes, the average was a 1.67, below “recommend to a friend”. The soups were a challenge for me, quite frankly, and there were various issues here associated with them. The bars were the best.

There was a comment Eric was making regarding sweetness, I found that the shakes were in general far too sweet. There's something going on there that is making them sweet. I'm not sure what it is. I wanted to provide some clarification in terms of what my view was on taste. Maybe this is something that you can leverage with some of your other patients or a much more scientific approach.

John Chant (43:27)

We have gotten feedback from other patients. I'm looking at your numbers. We're always looking to improve this.

One patient, and maybe it was you, said it felt overly sweet and like you're trying to disguise unpleasant flavor. That, unfortunately, is true. Single amino acids have a pretty strong taste. The other thing we learned is that people are completely different. I will agree with you. No one said, “This is the best food ever. I'm not going to eat regular food ever again.” That'd be ridiculous. We tried to rate these products as winners or losers. Every patient was vastly different. Some patients wanted to try every single one and vary their diet. Some patients would latch onto one, which I find hard to believe, but it's true, and eat only one for a whole month. They must have been very dedicated. That's our experience, but the point is well taken. I tasted all of them. Some I thought were pretty good. Some I did not like. We're doing our best at the moment.

Brian McCloskey (44:56)

I can imagine the challenges. I was trying to be candid because as a patient, having a good tasting product is like a ticket to play. If it's difficult to get down, then particularly when you're giving up a beautiful Sunday roast, or whatever it is, you have to make sure that there's a good tradeoff there.

John Chant (45:30)

People are not mice. Food creates additional challenges. Most people don't want to take this diet in December, or in late November, for obvious reasons. I just find it a fascinating challenge. We have to deal with human behavior, the human condition, and human desires. We can't change that. That's for sure.

Brian McCloskey (46:01)

The bars were good. It was like a 2.5. I applaud the efforts. Keep working on it.

John Chant (46:15)

A company from Europe spoke with us about partnering. I'm not sure they're interested. They said, “We looked at your website, and it seemed like you only have seven people.” This food was created by one guy, and so we can certainly do better.

One other interesting aspect of this is that monomer amino acids have a pretty unpleasant taste, some worse than others, if you just eat them. (Monomers are molecules that can react with other molecules to form very large molecules, or polymers. Amino acids are the monomers that make up proteins. Specifically, a protein is made up of one or more linear chains of amino acids, each of which is called a polypeptide.) That's what we have in the product. With all these synthetic food startups, it's a molarity thing (concentration in a solution). If you have all these monomer amino acids on your tastebuds, it's very strong, but if you put them into a polypeptide, proteins contribute to good flavorings. Our dream of the next generation product is that we would take the formula and put it into a polypeptide, so that the molarity and strong flavor would be gone. That would solve the problem. That's not happened yet.

Brian McCloskey (47:19)

Setting expectations for patients can go a long way. I found some times that the naming of the product might be a challenge because it is setting the expectation that you're going to get something, and then when you actually taste it, it may not.

John Chant (47:40)

That's interesting psychology. We have one we want to name “chicken noodle soup”. Everyone knows what chicken noodle soup is supposed to be. One of our products is borscht. I'm embarrassed to say I've never eaten borscht in my life. Our product scientist is Russian, and one of the subcontractors is Russian. I don't know what it’s supposed to taste like. Like beets? But if you say “chicken noodle soup”, you're setting yourself up. Because this isn't chicken noodle soup. We've had some interest in China, and we're considering making Chinese foods. Do you really want to follow the orthodoxy of the most popular foods? Maybe not, actually, because of what you're saying.

Brian McCloskey (48:31)

Trying to mimic it is a tall order. I know that you guys spent a lot of money to do it. But it's apparently a bit challenging.

John Chant (48:41)

Given a name, like “spicy pork wontons,” people in China would know what to expect, but maybe not people in the U.S. But if you say, “It's a peanut butter bar” in America, people would expect a certain taste.

Kevin Fordney (49:09)

I have an observation that you can respond to if you choose. Let's assume the food tastes really good. I applaud what you're doing. I’ve been more focused on treating the cancer, rather than the host, meaning me. Not that I eat horribly or anything else, but at this point, I haven't radically changed my diet or anything. But that idea is intriguing to me. I just have a hard time finding things that are compelling enough when this cancer journey is hard enough to begin with to do something radical. I understand it's early days, it's only been four or five years, and when I look at it that way, you've done a lot in a short amount of time. But for me, there's not enough evidence to where I would give up any other kind of treatment in order to put my faith in this. This is what I would see as what I'm missing, because I'm not a science person. At this stage, this feels more like a non-risk, no-side-effect supplement. If I want to try supplements, if there's some positive benefit, I may not even know how much came from this diet, and how much came from something else. I might be motivated to try this or something like it. But it doesn't yet fall under the treatment category for me.

John Chant (51:07)

We're gathering evidence from different patients who are at different stages and have different options therapeutically. We're not asking anyone to give up their therapy. We're saying this can be added to the therapy. We saw a signal in two patients among ten patients, or three patients in ten patients. I'm very excited about that. Absolutely early days. We're firing up to get 50 or 100 patients on this on again, off again protocol. It'll be pretty convincing. But we'll see.

Brad Power (51:49)

If I could just build on Kevin's point. You've got a focus group here. This is valuable for you to get this feedback, and we're happy to help you be successful.

What is your value proposition? What is the succinct one or two sentence, one paragraph version of why any of these patients should take a chance with your diet?

John Chant (52:20)

If we can convincingly show that this changes your rate of PSA rise for a sustained period, that's very valuable. PSA rise is used to determine what therapy they're going to get, in terms of whether it's going to be hormone reduction therapy, or chemotherapy, or an experimental therapy. It's all about longevity, of course, but it's also a benefit to your day-to-day life. We plan to do better. If we can slow the rise of PSA for a year or two, that's a tremendous benefit. Because your physician is guided by that.

Brad Power (53:21)

What's your go to market strategy? You've got a value proposition, you've got some scientific evidence, are you going Direct to Consumer, Direct to Patient? Word of mouth? What are you doing to attract patients?

John Chant (53:44)

That's not my area of specialty. I'm not a marketing person. In the oncology area, it's a pretty close community. The oncologists are very eager to have new ways of helping their patients, more so than in other fields. One way is scientific presentations at ASCO or the Prostate Cancer Foundation. We did one for the Prostate Cancer Foundation last year, but it was very early data. If we have compelling data that are published in a top journal, like the New England Journal, or one a little lower than that, it's compelling.

When you say word of mouth, we want to educate people by Facebook, or other groups.

For medical food, it's not a therapeutic, but under FDA regulations, it has to be under the supervision of a physician, so we do have to educate the physicians, but indirectly, by going directly to the customer also, because unless the patient's asking for something that's outrageous or dangerous, the physician will approve it. We have a lot of work to do.

Eric Hall (55:11)

Have you spoken to or met with oncologists that are on board with this? I've met with five different medical oncologists, and none of them have liked my questions around nutrition. When I asked about nutrition, they say it has no impact on healing your cancer. That's something I've

stumbled across. They seem to just want to give me prescription medication. So I'm wondering, following up with Brad's question about your vision as far as getting this into the oncologist world as an accepted form of treatment by them?

John Chant (56:01)

The oncologists we've spoken to have been pretty receptive. In our small study at Stanford, a lot of oncologists there who weren't involved in the study are very interested also. As I said at the start, there's a patchy history of supplements and cancer and supplements and health. But to dismiss wholeheartedly nutrition as having any role is a little outrageous. A lot of physicians are interested, some will not be, of course. We're not asking people to give up their therapy or their medicine; this can be added to it. It will add one other thing. There was an interesting study that came out of Korea a few years ago, where they showed that if patients were given, and this is not therapeutic intervention, very good nutrition support, it had an improvement on survival. The doctor saying this or that to you versus intensive support made a difference in survival. That's not a therapeutic effect. That's the host effect, or whatever you want to call it, your body being stronger.

Eric Hall (57:30)

You're spot on with that comment. I'm doing some diet and supplement things. Some of them are for anti-cancer benefits. Some of them are just to boost my immune system on my body to help support me dealing with whatever other treatments.

John Chant (57:45)

It's undeniable that if your body is stronger, you're going to do better..

Ken Anderson (58:01)

Eric, you're absolutely right. I've chatted with a half a dozen medical or genomic doctors, and they have absolutely no interest in learning about nutrition. Most of them are so wrapped in what they're doing. They'll send you to the nutritionist on staff to talk about your diet. But when I first got diagnosed in 2017, I reached out to more than a dozen guys that were ten plus years on the overall survival curves, at the tail end of that overall survival curve for advanced prostate cancer guys, and without exception, all of them had the same the comments: exercise and stop red meats, dairy, and alcohol. And those are the guys that were still around after 10 years. I strongly believe, and a lot of guys that I chat with today, say diet is key, but their doctors say diet has no place, but it's absolutely impossible for me to believe that.

John Chant (59:07)

Diet has a place in all parts of human health.

Ken Anderson (59:14)

I don't know how you're going to get the doctors on board or I don't know where it's going to go, but it definitely helps in regards to overall quality of life. Losing 20 or 15 pounds when you're 60 years old is not a bad thing.

John Chant (59:40)

I'm 59, and my grandfather had prostate cancer. My father had prostate cancer, and my education is a PhD in genetics. It's a personal interest.

Brad Power (59:55)

On metabolic testing, which you mentioned: we had a session with Robert Nagourney, who is doing metabolic testing. Is the pathway, or the method of action that we're presuming here is that there's something between the food you eat and feeding the cancer, and you're going to interrupt that pathway? It seems that you could have metabolic testing somewhere, as an intermediate biomarker, to see if we are affecting the system. It's metabolic, like feeding glucose to the cancer. We had a very complicated explanation about using mass spectrometry to develop pathways, and it blows my mind, but it's essentially a model, a mental model of how it goes from one thing to another. We have other mental models, such as that it goes from DNA -> RNA -> proteins. I'm curious about the pathway model, and whether you could interject testing that would look at an intermediate biomarker, that would be something other than the outcome of like a reduction in PSA?

John Chant (1:01:23)

We have a lot of data. We're not looking at everything because there are many metabolites in the blood. I showed you one patient where his PSA went down at the time we added the diet. The other one was stabilized and went down. We were looking at all the amino acids in their blood. The hypothesis is that you lower an amino acid, and then that starves the tumor. For those amino acids that don't go down, those are probably not the ones mechanistically involved. There are certain amino acids that are more implicated in cancer. A lot of this is published. We've published also. For the patients who appeared to have a response, the amino acids that are front and center, in terms of the thoughts about feeding cancer in the literature, were the ones that went down. So that's encouraging. The other thing I will tell you, and it's published in our paper, mechanistically, it's not just starving them and slowing them down, it appears that when they get reduced amino acids of certain types, that they will go into an apoptotic (programmed cell death) pathway, so there will be some alarm in the cell, and some of the cells will die. That's about as far as we know. We think it is an active mechanism, rather than slowing them down. We plan next year to do a big study, with maybe Mike Snyder's lab or another lab, where we will look at patients and then look at everything. We will look at the hundreds of metabolites in the blood. I'm sure that'll be very fascinating. Looking at all the amino acids has been tremendously fascinating also. We generate a lot of data, but we don't know with certainty.

“Starving Tumors with a Therapeutic Diet” (John Chant) [#36]

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Chat Notes

Saed Sayad: A good read:
https://scitechdaily.com/anti-tumor-effects-without-toxicities-researchers-use-a-spice-to-treat-cancer/

Stephanie Hall: Just wanted to say that I agree that there is an established strong connection between the uptake and metabolism of amino acids and cancer cells. And there have been a lot of studies looking into metabolic reprogramming. If one were to search you’d find lots of info on depleting Glutamate because cancer cells feed on that (or asparagine, glycine, cysteine, etc). Here’s one example https://www.frontiersin.org/articles/10.3389/fcell.2020.603837/full

And by “if you do a search” I mean patients who might want to present this to their oncology team

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7071719/

“Starving Tumors with a Therapeutic Diet” (John Chant) [#36]

John Chant Follow-up on the Question on Carbs and Sugars

In the meeting Filtricine was asked about carbs and sugars in their products.
Here is some detail on the composition of their diet.
They welcome feedback.

Macronutrients and Calories in Tality

	SOUPS 1 bag-100g			SHAKES 1 bag-100g			BARS 1 bar -54g		
	g	Cal	% Cal	g	Cal	% Cal	g	Cal	% Cal
Fat	12	108	27.84%	12	108	27.84%	7	63	31.03%
Protein	15	60	15.46%	15	60	15.46%	7	28	13.79%
Total Carbohydrates	61	220	56.70%	61	220	56.70%	30	112	55.17%
Total:	n/a	388	100.00%	n/a	388	100.00%		203	100.00%

Notes: Fat has 9 cal/g, Protein has 4 Cal/g, Carbohydrates have 4cal/g
Sugar and fiber are kinds of carbohydrates and included under Total Carbohydrates
Sugar has 4 Cal/g (included in calculations). Fiber is indigestible and has no calories.

Calories from Carbohydrates Breakdown

	SOUPS 1 bag-100g			SHAKES 1 bag-100g			BARS 1 bar -54g		
	g	Cal	% Cal	g	Cal	% Cal	g	Cal	% Cal
Complex Carbohydrates (maltodextrin)	49	196	89%	44	176	80%	17	68	61%
Sugar	6	24	11%	11	44	20%	11	44	39%
Fiber	6	0	0%	6	0	0%	2	0	0%
Total Carbohydrates	61	220	100%	61	220	100%	30	112	100%

From Xiyan Li:

Regarding information about dietary fiber and added sugar under Total Carbs, below are the Nutrition Facts labels for shakes, soups, and bars.

We always send this information to prospective patients before their consent.

“Starving Tumors with a Therapeutic Diet” (John Chant) [#36]

COCONUT DATE BAR

Nutrition Facts	
1 serving per container	
Serving Size	**1 bar (54g)**
Amount Per Serving	
Calories	**200**
	% Daily Value*
Total Fat 7g	9%
Saturated Fat 3.5g	18%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 55 mg	2%
Total Carbohydrate 30g	11%
Dietary Fiber 2g	7%
Soluber Fiber 2g	
Total Sugars 11g	
Includes 10g Added Sugars	20%
Protein 7g	

MOCHA CHOCOLATE CHIPS BAR

Nutrition Facts	
1 serving per container	
Serving Size	**1 bar (60g)**
Amount Per Serving	
Calories	**220**
	% Daily Value*
Total Fat 8g	10%
Saturated Fat 4.5g	23%
Trans Fat 0g	
Cholesterol 0mg	0%
Sodium 55mg	2%
Total Carbohydrate 33g	12%
Dietary Fiber 2g	7%
Soluber Fiber 2g	
Total Sugars 14g	
Includes 13g Added Sugars	26%
Protein 7g	