“A Unique Personalized Killer T-cell Treatment for Glioblastoma" (Wayne Carter, DVM, PhD) [#110]

Brad Power
August 21, 2024

“We're educating your immune system so it recognizes your own tumor, and then it can eliminate it.” – Wayne Carter, DVM, PhD

“This is a personalized therapy. As opposed to saying it's an engineered technology, I would say, instead, it is completely personalized to the individual patient and thus, we believe it can potentially treat any cancer.” – Wayne Carter, DVM, PhD

Meeting Summary

Patients with difficult-to-treat cancers, such as glioblastoma, see immunotherapies as offering one of the best paths to a durable response. An immunotherapy fights the cancer system with the immune system, and the side effects can be more appealing than the side effects of other treatments, like chemotherapy, which weakens the immune system. One immunotherapy is a personalized cancer vaccine, which is attractive because it offers a possible treatment option to nearly every cancer patient. Personalized cancer vaccines can be used to introduce or stimulate selected T cells (a kind of white blood cell, part of the immune system) to attack cancer cells. A personalized cancer vaccine leverages the immune system's ability to see self/normal versus non-self/foreign cells and attack the non-self/foreign cells through a tailored antitumor response to their tumor mutation signature. The vaccine is trying to get your body to produce enough of the right T cells, and then combine it with other personalized drug combinations to make sure that those T cells can do their job and win the battle against the tumor. Another immunotherapy technology that is similar is “tumor infiltrating lymphocytes” (TIL), where they take your tumor sample, find the T cells that are in that sample, verify that those T cells are the ones that are supposed to be there doing the job, then expand those and inject them back into the patient.

Wayne Carter, DVM, PhD, President and CEO, TVAX Biomedical, is uniquely qualified to discuss the cutting edge of immunotherapy technologies. TVAX Immunotherapy® uses your T cells to fight your cancer. The key distinction of the TVAX Immunotherapy® is that it uses both a cancer vaccine pre-treatment to generate cancer-specific T cells and an activated “killer” T cell treatment. This proprietary immunotherapy approach has demonstrated efficacy against numerous cancers with low toxicity. TVAX Biomedical received Fast Track Designation from the FDA for TVAX Immunotherapy®. Their first application of the technology is in glioblastoma multiforme (GBM). Dr. Carter has more than 18 years of Fortune 500 experience in pharmaceutical and nutrition R&D. In his role at Pfizer as Executive Director of Global Clinical Development, he accelerated the development of many drugs using novel clinical technologies. His board appointments include MRI Global and Acenxion Biosystems. Dr. Carter received his B.S., D.V.M., and Ph.D. in Immunology from Purdue University.

How does your immune system fight cancer?

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The immune system has evolved to protect us from pathogens such as bacteria, viruses, and fungus. When an infection arises, the immune response is triggered, all of the infection is eliminated, and then the immune response goes back down. But a memory of the infection persists, and you get a healthy memory cell, so that if you see that pathogen again, it can react quickly. But that doesn't happen in cancer, because if the tumor doesn't completely go away early in the process, the immune cells become exhausted, and are just not as functional. So they may need to be reactivated, or even worse, the immune system never saw the tumor in the first place, because tumors can be clever, perhaps able to block recognition by the immune system. So there are a lot of hurdles: tumor evolution, tumor heterogeneity, different cells expressing different things and then this exhaustion phenomenon from the cells seeing the antigen too much.

How do immunotherapies work to treat cancer?

Immunotherapies (a treatment leveraging your immune system) offer one of the best paths to a durable response -- they are fighting a biological system (your cancer) with another system (your immune system), rather than the hit-and-miss, less durable approach of targeting a biomarker with a single drug or poisoning your cancer with chemotherapy. The idea is to try to find what's different about the tumor that is allowing it to avoid the immune system. Sometimes the tumor turns things back on that are generally turned off in people, sometimes it turns up the volume on things that are generally turned down. So if you can find these reactivated genes, you can perhaps get the immune system to recognize them and attack them. But the immune system doesn't usually recognize them without a vaccine because a successful tumor shields itself from the immune system by being a terrible antigen-presenting cell. Immunotherapies offer a treatment option to nearly every cancer patient because they are neither targeted to a specific “tissue of origin”, like lung cancer or colon cancer, nor are they targeted to a biomarker, a protein that your cancer cells overexpress, like BRCA or EGFR.

What is the TVAX immunotherapy approach and how is it different from other immunotherapies?

- The TVAX approach isolates and inactivates the tumor cells, vaccinates patients with these cells, collects primed T cells from the patient via leukapheresis, activates and expands the T cells and then infuses activated effector T cells into the patient.
- The TVAX approach is different from other immunotherapies you may have heard of and considered, such as (1) immune checkpoint inhibitors (e.g., Keytruda/pembrolizumab, OPDIVO/nivolumab), (2) CAR-T (chimeric antigen receptor T-cell) therapy, or (3) personalized neoantigen vaccines. It is closer to a (4) “TIL” therapy (Tumor Infiltrating Lymphocytes), which takes T cells found near your tumor, grows them in a lab, and infuses them into you.
- The TVAX technology is a “polyclonal cancer neoantigen-specific adoptive T cell therapy” – which is a mouthful of medical jargon. Let’s break it down:
    - *Polyclonal*: antibodies produced by multiple immune cells, or in this particular case multiple T cells derived from different tumor antigens.
    - *Cancer neoantigen*: a new protein that forms on cancer cells when certain mutations occur in tumor DNA

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    - *Adoptive*: taking your healthy cells, e.g., white blood cells, growing them in a lab, then putting them back into your blood
    - *T cell therapy*: a type of immunotherapy that makes your immune cells better able to attack cancer
- A big advantage of expanding your own T cells and then infusing them back into you is that you don’t have problems with the side effects of rejection by your immune system which come from engineered therapies.
- The TVAX therapy has shown promising results in dogs with bone cancer, extending median survival from 4-10 months to 1900 days. In human trials, 20% of patients lived five years or longer, with a median survival of 17 months. The therapy is currently in a 120-patient study, focusing on newly diagnosed MGMT-negative patients. They are recruiting patients. The therapy aims to be competitive in cost, potentially undercutting existing CAR-T therapies.
- The TVAX time from “vein to vein” – from collecting your T cells to expanding and reinfusing them – is seven days. For personalized neoantigen vaccines the design and manufacturing can take several months, and for CAR-T it is typically three to five weeks.

When should you consider getting immunotherapy?

Many immunotherapies are still experimental. Most doctors will recommend that you should get the standard of care first and try something experimental later. The problem with that, for immunotherapy, is that you need your immune system to be able to respond. If you get chemotherapy, radiotherapy, steroids, or other standard treatments, your immune system is beat up. If you can, it would be better to get immunotherapy first. If you’ve had standard treatments, you should try to reset your immune system as best as you can to be able to get the most from a cancer vaccine or immunotherapy.

As a tumor gets larger, it starts to get more heterogeneous and more diffused and spread out across multiple sites in the body. The microenvironment is more suppressive to the immune system. Therefore the timing for trying immunotherapy is probably better when you have less cancer, or at an earlier stage.

How can you access the TVAX immunotherapy?

- You can enroll in the current clinical trial if you have glioblastoma, are newly diagnosed (before surgery and have not been on other treatments), are MGMT negative, and have a cubic centimeter of fresh tissue.
- You can potentially access it on an emergency use basis. Ideally, you should not yet have had chemotherapy or radiation, so you have a strong immune system.
- You need a centimeter cubed of fresh tumor tissue.

What’s next for TVAX and immunotherapy?

- Apply the therapy to other cancer types once glioblastoma approval is achieved
- Combine the T cell therapy with other approaches like checkpoint inhibitors or Optune
- Combine with an oncolytic virus
- Add in more doses of T cells
- Educate patients, caregivers, and physicians that the more we can maintain the integrity of the immune system, the better patients are going to be able to fight their cancer

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How can you learn more?

- For more on immunotherapies for cancer treatment, please see our discussions with:
    - Lisa Butterfield on cancer vaccines here
    - Willy Hoos on personalized neoantigen vaccines here
    - Gary Onik on personalized in vivo immunotherapy for “cold” cancers here
    - BostonGene on predicting immunotherapy response with a diagnostic test here
    - Sumit Subudhi on immunotherapies in prostate cancer treatment here
    - Matthew Dons on growing your white blood cells here
- For more on TVAX, please contact Wayne Carter at wcarter@tvaxbiomedical.com.

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Meeting Notes

KEYWORDS

t cells, patients, question, antigens, vaccine, tumor, cancer, vaccination, immune system, cells, therapy, study, immunotherapy, surgery, response, technology, treatment, gbm, cancer cells, recurrent

SPEAKERS

Wayne Carter (69%), Brad Power (13%), Chris Apfel (7%), Gitte Pedersen (3%), Richard Anders (2%), Roger Royse (2%), Robb Owen (2%), Allen Morris (2%), Mark Stoner (1%), Brian McCloskey (1%)

ADDITIONAL CHAT PARTICIPANTS

Bill Paseman, Ryan Moon, Martin Luzbetak, Vanessa Hugo

SUMMARY

Wayne Carter discussed TVAX, a startup with an innovative approach to a personalized immunotherapy for cancer, specifically glioblastoma. The technology involves isolating and attenuating tumor cells, vaccinating patients with these cells, and then infusing activated T cells. The therapy has shown promising results in dogs with bone cancer, extending median survival from 4-10 months to 1900 days. In human trials, 20% of patients lived five years or longer, with a median survival of 17 months. The therapy is currently in a 120-patient study, focusing on newly diagnosed MGMT-negative patients. They are recruiting patients. The therapy aims to be competitive in cost, potentially undercutting existing CAR-T therapies.

OUTLINE

Introductions: Wayne Carter and TVAX Overview

- Wayne Carter is based in Athens, Georgia, and his company is headquartered in Kansas City.
- The focus initially is on glioblastoma, and in the future a wider applicability of the technology.
- The technology uses T cells, which bind to cancer cells.
- The therapy is personalized, not engineered, and has the potential to treat any cancer due to its personalized nature.
- The technology is a polyclonal cancer neoantigen-specific adoptive T cell therapy.
- They have fast track designation by the FDA for newly diagnosed glioblastoma.

Technology and Clinical Benefits

- The process: a surgeon removes a tumor, cells are isolated, attenuated with radiation, combined with GM-CSF, and vaccinated into the patient.
- The immune system responds.

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- T cells are primed against the cancer.
- A study on dogs with bone cancer showed significant survival benefits with immunotherapy.
- The USDA Center for Veterinary Biologics approved the treatment of bone cancer in dogs.

Human Clinical Study and Current Study Design

- A study on recurrent high-grade glioma showed improved survival with the therapy.
- Treating patients with a healthy immune system and minimal residual disease is best.
- The current study design focuses on newly diagnosed MGMT-negative patients with minimal residual disease, with inclusion criteria, timeline, and the control group receiving adjuvant temozolomide.

Q&A Session: Timeline and IL-2

- Brad Power asks about the timeline and adjuvant therapy choices, and Wayne explains the design based on expert consultation.
- Brad Power inquires about the use of IL-2, and Wayne explains its role in continuing T cell expansion in vivo.
- Robb Owen asks about treatment options for his friend with glioblastoma, and Wayne explains the emergency authorization process.
- Gitte Pedersen asks about the selection of new antigens, and Wayne explains the polyclonal approach and the use of whole cell suspensions.

Q&A Session: Cost, Adverse Events, and Clinical Trial Design

- Richard Anders asks about the cost of the therapy, and Wayne explains the competitive pricing compared to existing CAR T therapies.
- Richard Anders inquires about autoimmune manifestations, and Wayne explains the lack of such issues due to the use of the patient's own T cells.
- Richard Anders asks about the clinical trial design, and Wayne explains the decision to go with a one-to-one randomized trial.
- Brad Power answers a question about the duration of the therapy, and Wayne explains the seven-day vein-to-vein time and the potential for expansion.

Q&A Session: Immune Response and Combination Therapies

- Roger Royce asks about the immune response, and Wayne explains the use of delayed-type hypersensitivity (DTH) response.
- Brian McCloskey asks about pre or post immune profiling, and Wayne explains the focus on getting an approval first.
- Vanessa Hugo asks about the therapy's potential, and Wayne explains the limitations due to the pre-surgery trial enrollment requirement.
- Wayne discusses the potential combination with Optune and checkpoint inhibitors.

Q&A Session: Technical Questions and Recruitment Challenges

- Chris Apfel asks about the vaccination process and the number of cells injected, and Wayne explains the use of anti-CD3 and the rationale behind the vaccination schedule.

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- Chris Apfel inquires about the possibility of getting the therapy outside the study, and Wayne explains the emergency authorization process.
- Chris Apfel asks about the recruitment challenges, and Wayne explains the issues with fresh tissue and the need for more sites and neurosurgeons.
- Chris Apfel asks about the long-term survival benefits, and Wayne explains the importance of maintaining the immune system's integrity.

Q&A Session: Additional Questions and Future Directions

- Brad Power asks a question about the dose of IL-2, and Wayne offers to provide the details via email.
- Ryan Moon asks about treating diffuse intrinsic pontine glioma, and Wayne explains the intention to focus on recurrent GBM if approved.
- Brad Power answers a question about treating kidney cancer, and Wayne suggests combining the therapy with checkpoint inhibitors.
- Wayne concludes by emphasizing the need for significant funding and the potential for the therapy to treat many different cancers.

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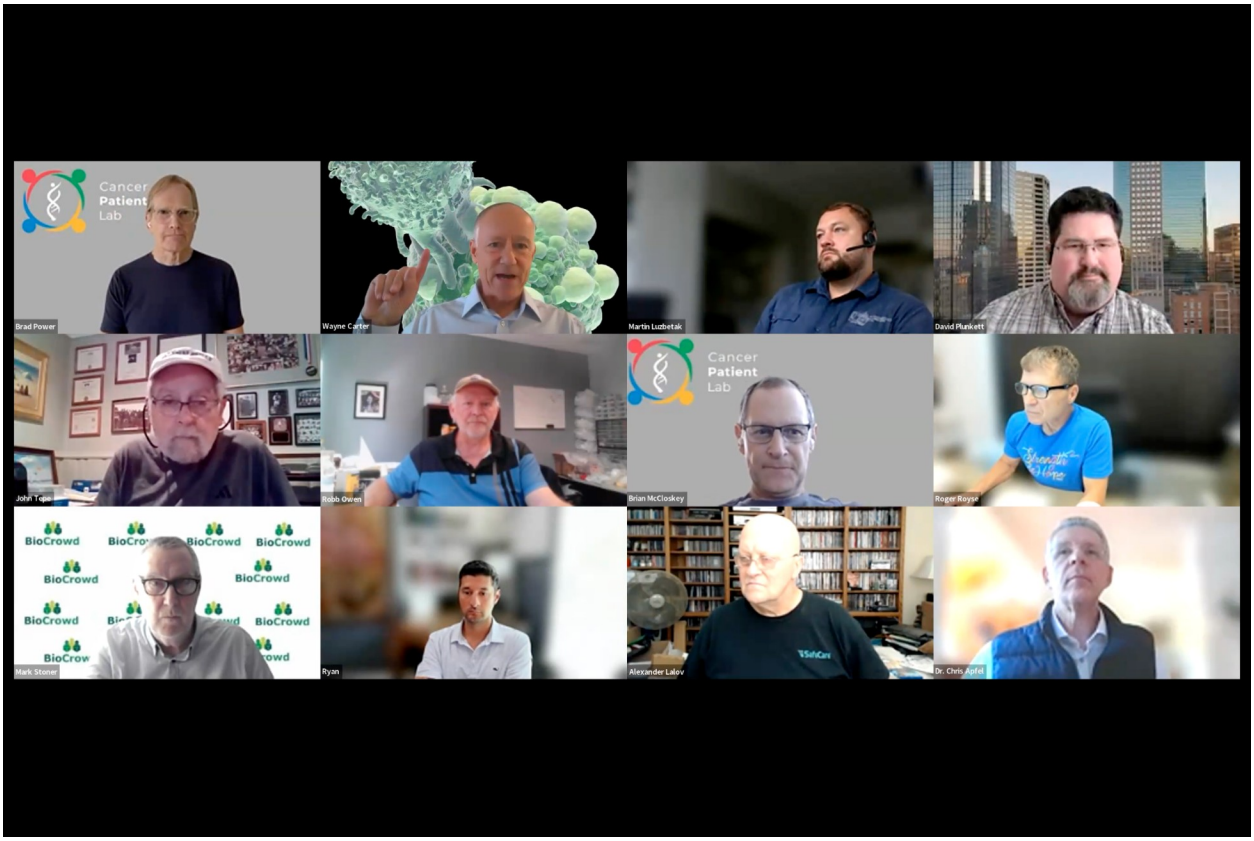
TRANSCRIPT

Brad Power
This is the Cancer Patient Lab.

We're honored today to have Wayne Carter with us. He's going to tell us about technology and a startup that he's leading that has an innovative approach to immunotherapy, an engineered immunotherapy, which is a big opportunity that a lot of folks are very interested in. Let me just handle the housekeeping items first. There are three that we just typically do at the beginning. This is for information purposes only. This is not medical advice. We try to arm patients and caregivers with information that they can take to their medical team. The second is that this is all public. Everything you say can and will be made public. So if you're concerned about that, hide your image, change your name and don't say anything. And finally, we are a nonprofit, patient led community, learning community, and we'll appreciate any donations that people might make, and you can do that through our website. And with that, I'll turn it over to Wayne, just to introduce Wayne briefly, as he was just saying, He's based in Athens, Georgia, it always helps me to locate where people are. But his company is headquartered in Kansas City, which is, I think, where David Plunkett is, and they've got a novel approach to an engineered immunotherapy. I was introduced to Wayne by Chris Schuler, who introduces me to somebody every week, practically, it seems, who really knows his way around brain cancer. They're starting in glioblastoma, but their technology can have wider applicability to a number of cancers.



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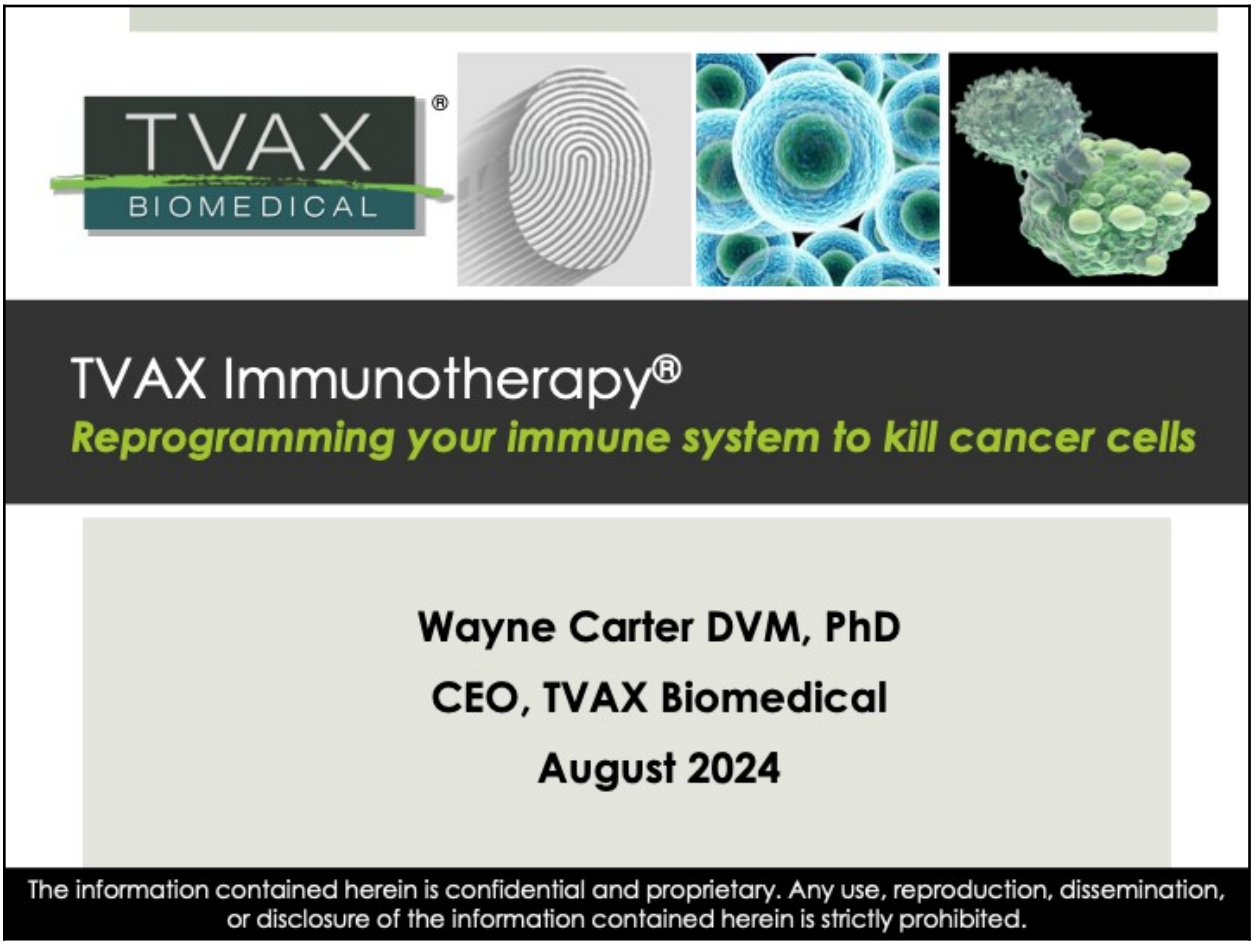
Wayne Carter 1:58
I am going to start with the image behind me because you may have interest in it. This is a T cell, and you can see this T cell is sending these long finger-like projections, and it's binding to the cancer cell, which is behind me, and then injecting toxins into that cancer cell and killing it. That cancer cell is undergoing apoptosis (cell death), and that is the essence of our technology.



I want to clarify one thing: these are not engineered. This is not a genetically-modified therapy. This is a personalized therapy. As opposed to saying it's an engineered technology, I would say, instead, it is completely personalized to the individual patient and thus, we believe it can treat potentially any cancer, because it is so personalized. That is why we have the thumbprint up here to represent that personalization.

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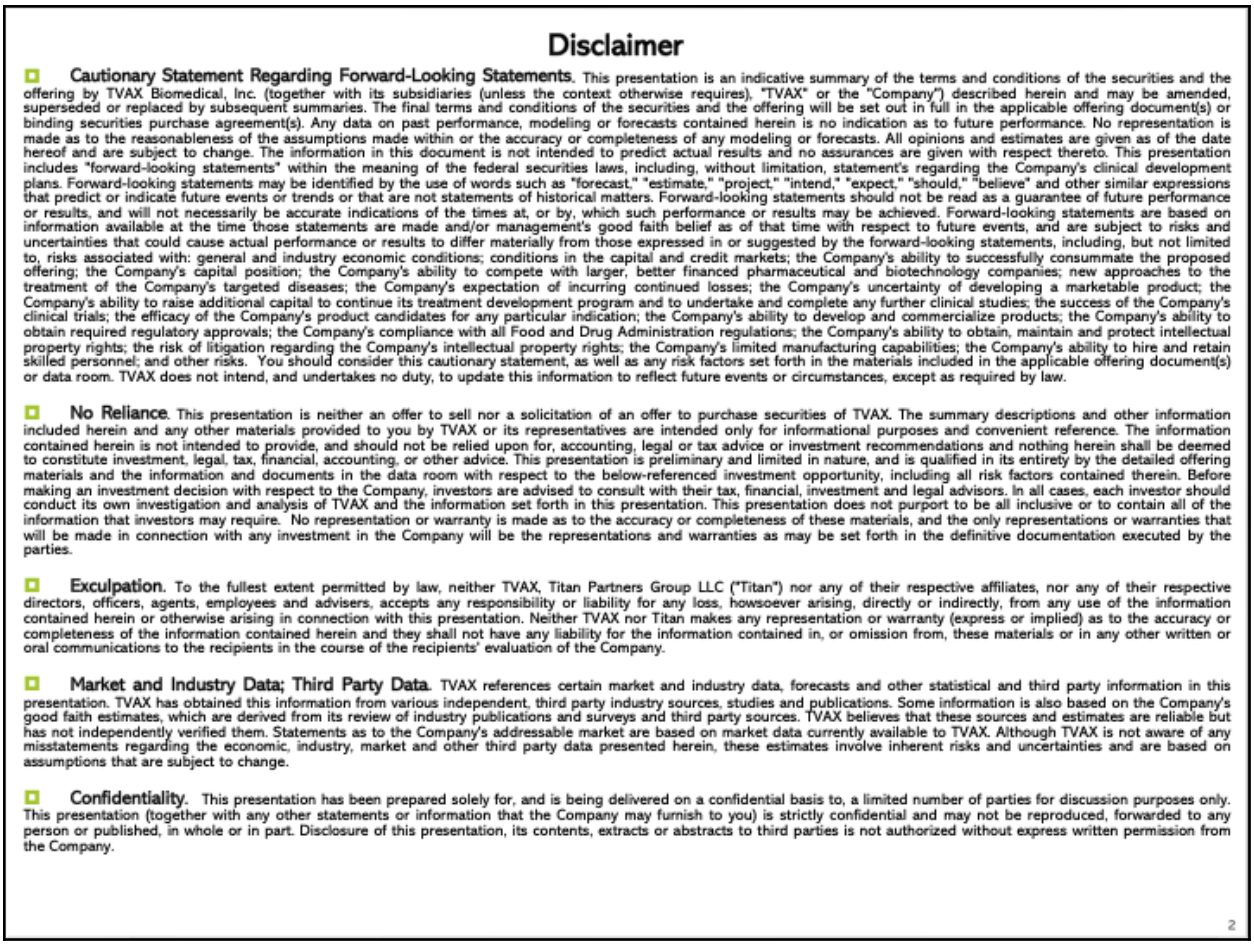

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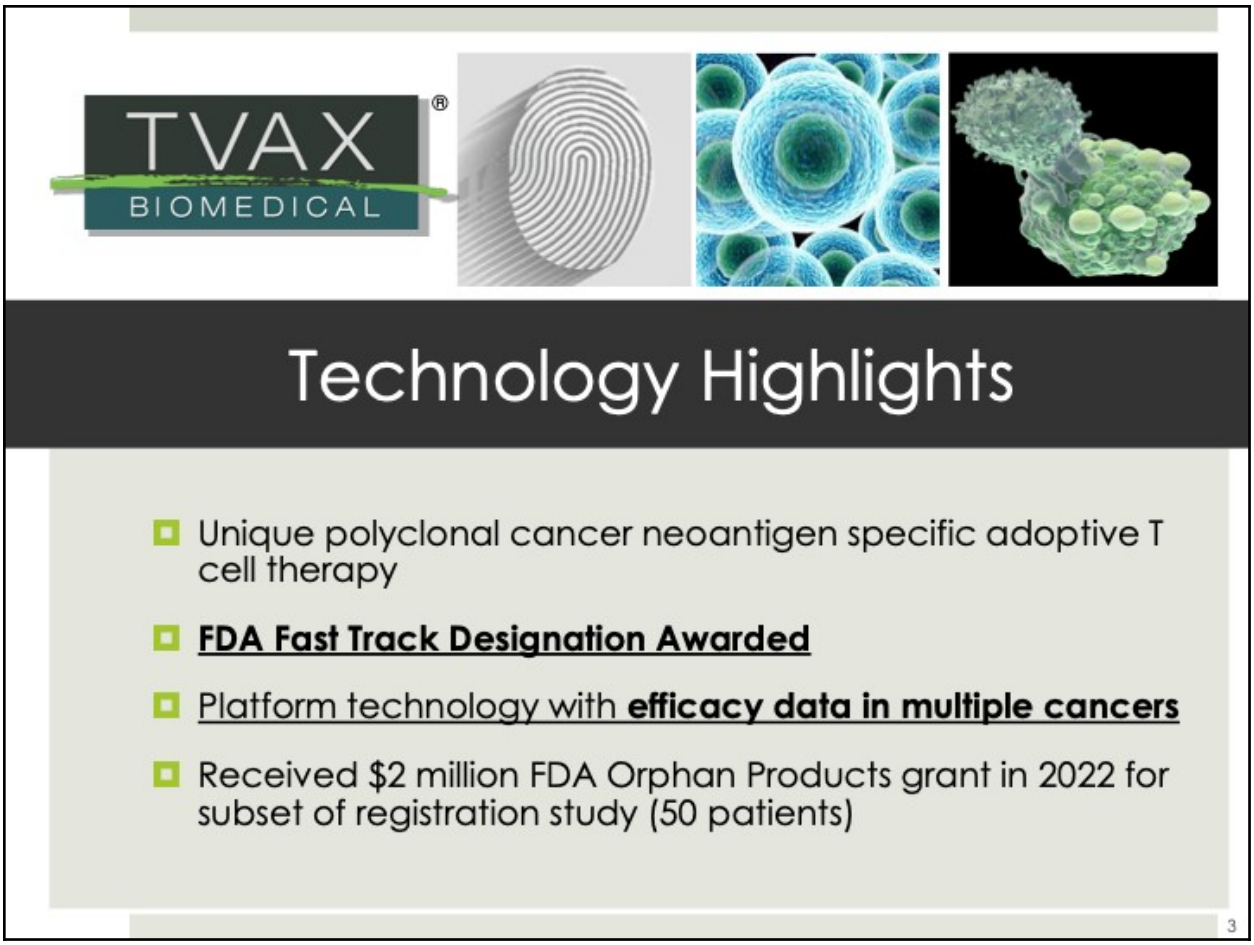

This is a quick highlight. If you put a name to it, our technology is a polyclonal cancer neoantigen specific adoptive T cell therapy. I’m happy to dig into that. We have fast track designation, which has been given to us by the FDA for newly diagnosed glioblastoma. We do believe it's a platform technology because it is so personalized.

I'm going to show you some of the data which represents the broad applicability of this. I'm not going to show you data in Stage Four renal cell carcinoma patients today. But again, we do believe it's a platform technology. We have received a $2 million grant from the FDA office of orphan products to help develop the technology.

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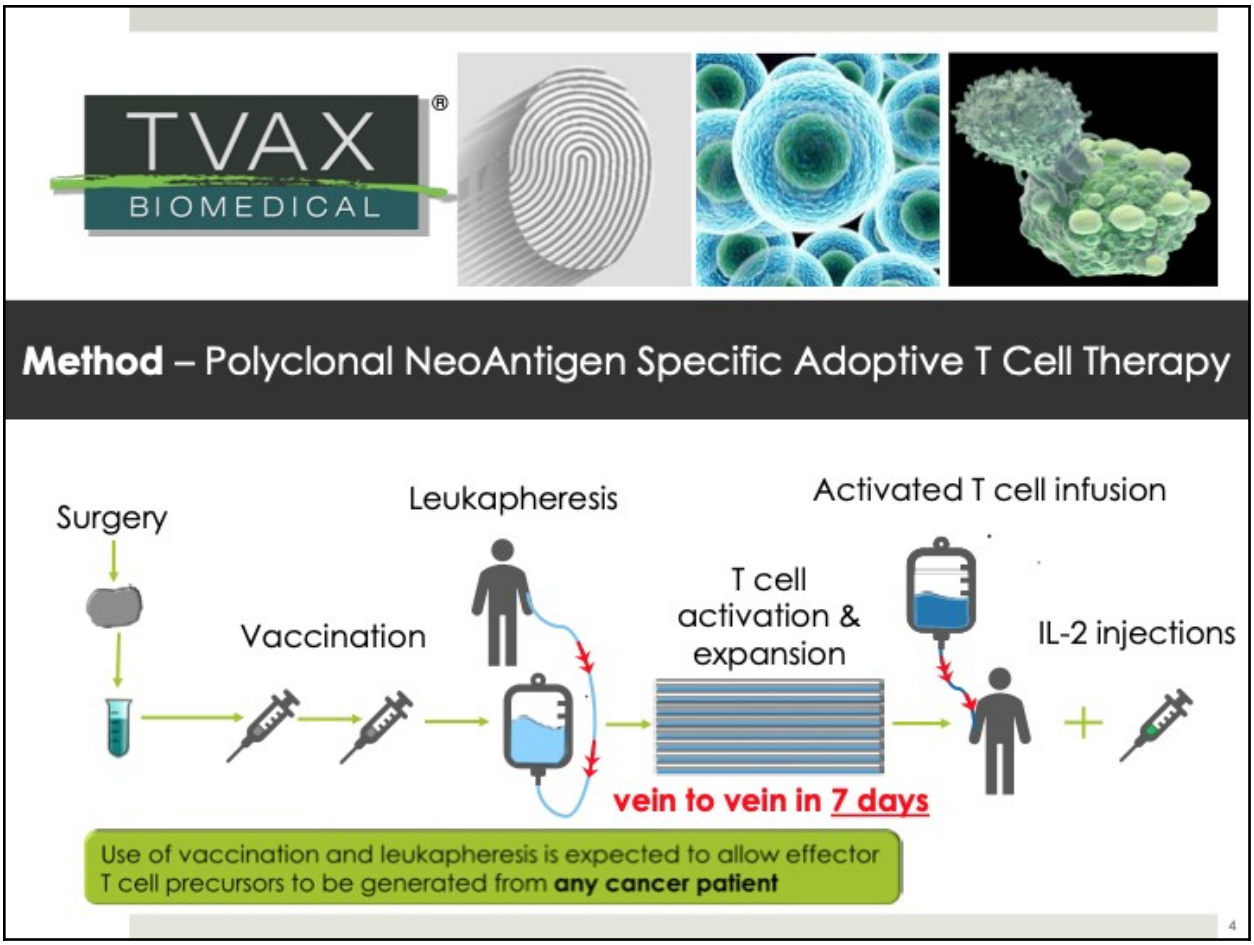


This is the way that the technology works:

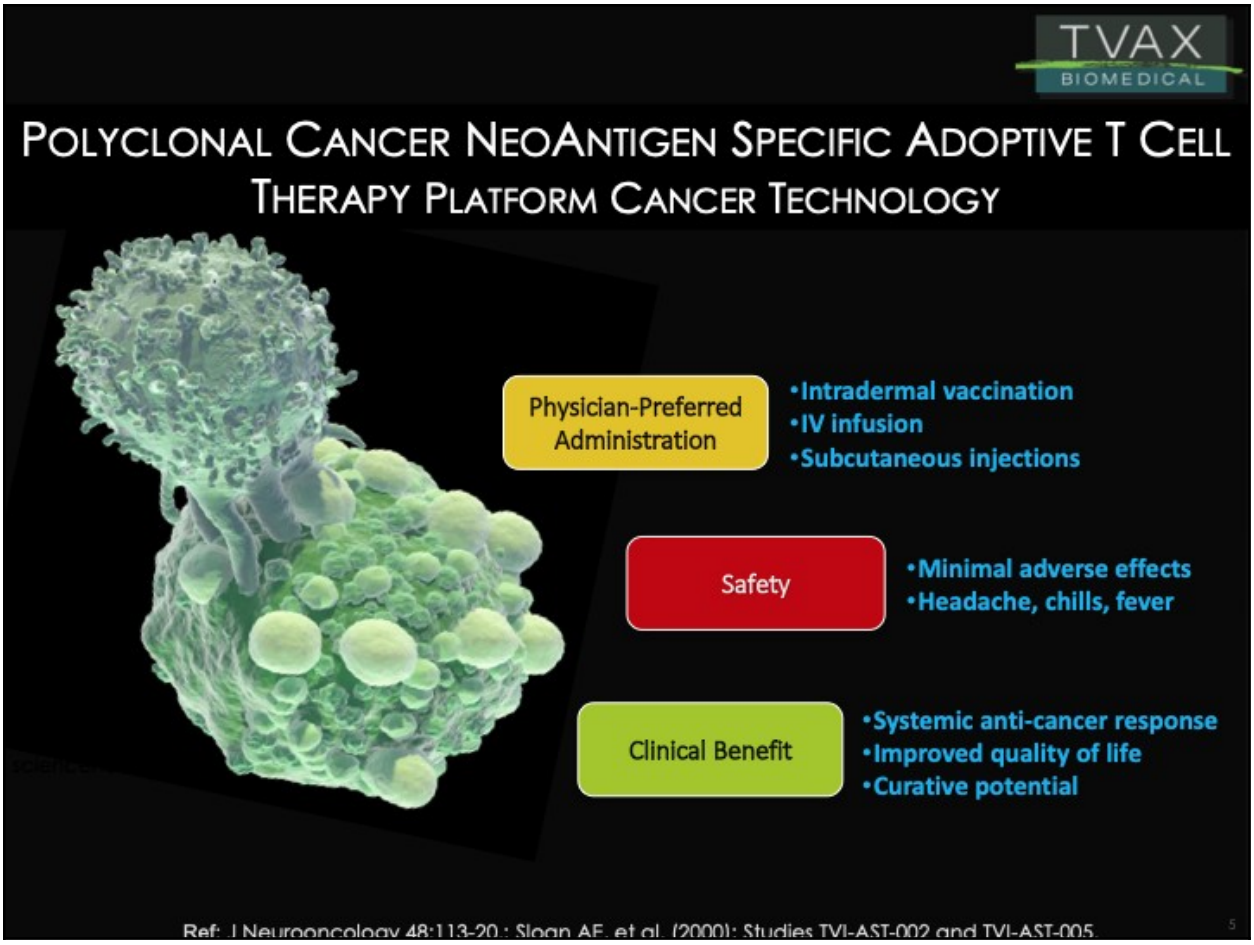
1. The surgeon removes the tumor.
2. That tumor gets sent to our manufacturing facility. There, we isolate about 50 million cells from that tumor.
3. We then attenuate (weaken or thin) the cells with 50 Gray of radiation so they're still alive, but they're no longer capable of growth or replication.
4. We then combine those cells with GM-CSF (Granulocyte Macrophage - Colony Stimulating Factor, to elicit antitumor and antiviral immune responses), which is an adjuvant (a substance used to increase the efficacy or potency of certain drugs).
5. We vaccinate the patient twice against their own cancer.

You generally don't have a good immune response against your cancer. Cancer has figured out how to evade our immune system. So this is really the first time that you will have a good immune response against your cancer. We also know that there have been literally hundreds of failed vaccination trials, and vaccination, by itself, generally, is not enough to cure your cancer. We're doing vaccination in this therapy to prime your T cells against your cancer. We then collect those primed T cells via leukapheresis (a blood draw that separates out the T cells and returns the rest of your blood), and that leukapheresis sample gets sent again to our

manufacturing facility. We activate and expand those T cells and then infuse them back into the patient, giving back, generally, about 50 billion activated effector T cells, and then follow that up with low dose IL-2 injections.

Those T cells will literally circulate throughout your body and identify the cancer, just as I described at the start, and then bind to it and then kill it and bring in other cells which are capable of killing those cancer cells.

Our vein-to-vein time is about seven days, which is really quite good, but I'm going to explain in the glioblastoma study why we actually have a greater separation between leukapheresis and the T cell infusion.



This is an overview slide.

It’s easy for physicians to administer.

We have a very favorable safety profile. These are your own T cells. They're not genetically modified, and so there are really very few side effects associated with this therapy.

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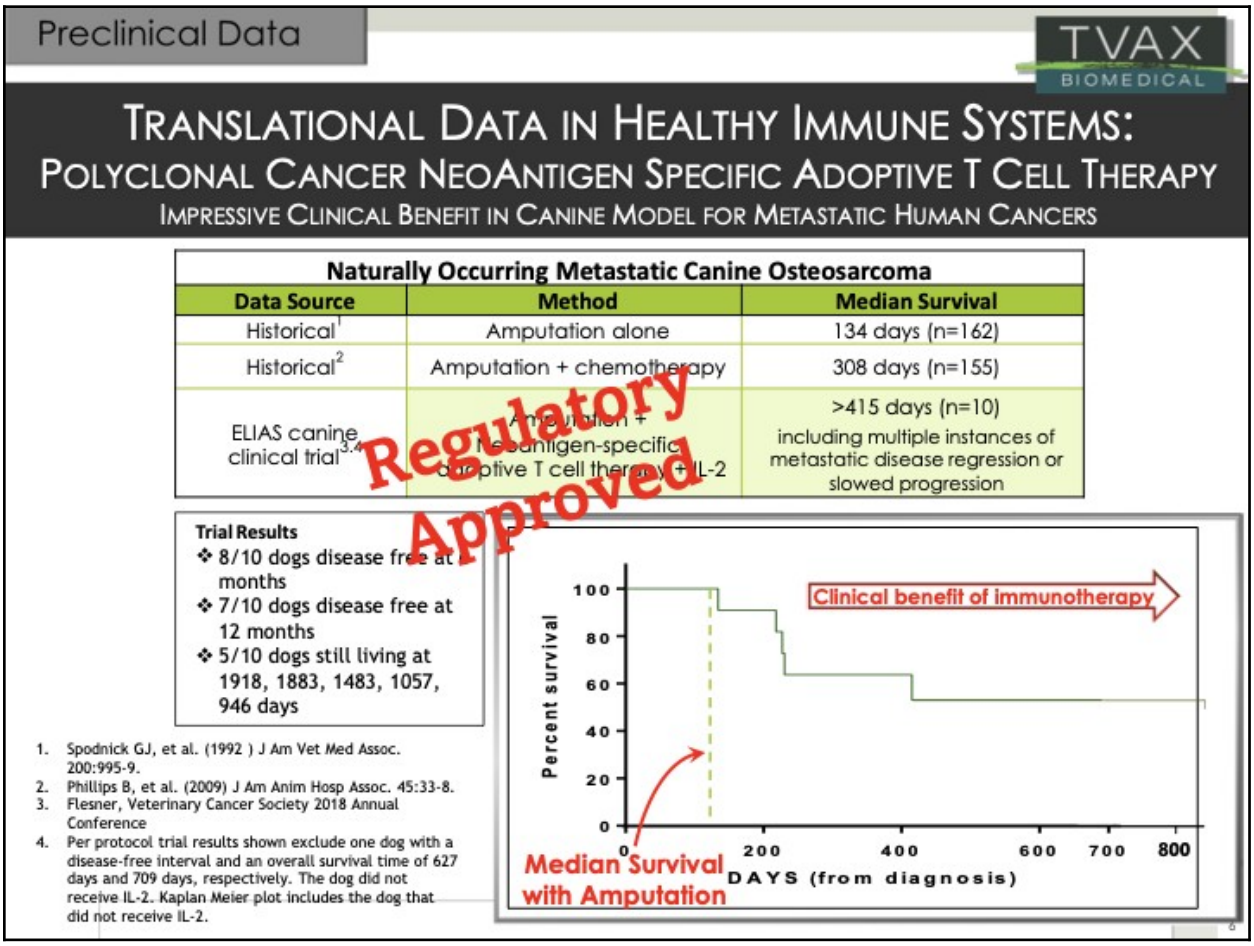
Next, I'm going to show you some of the clinical benefits.



We have a sister company, and that sister company is focused on animal health. It’s the same technology, but it's being used for dogs, and in this case, dogs with bone cancer. Dogs get bone cancer, osteosarcoma, just like people do. When they get it, they're usually dead within a couple of months. You can do amputation, and they'll live about four months. You can do amputation and aggressive chemotherapy, and they'll live about 10 months. In this study, we did amputation followed by the immunotherapy.

This vertical line in this Kaplan Meier curve represents the median survival that you would get with amputation alone. Obviously you can see there's a lot of survival that's occurring beyond that, and that's really the benefit of the immunotherapy. This was a two year study, and as you can see, half of the dogs were alive at the end of that two year study. They went on to live many months and years thereafter. The survival of those five of the 10 dogs went out to almost 2000 days, 1900 days, 1500 days, 1000 days, etc. These were old dogs to start with. This is naturally occurring bone cancer. This was not a contrived model. This bone cancer developed naturally in these dogs. It was quite a significant therapeutic benefit in these dogs. For all practical purposes, we believe that several of these dogs may have been cured of the bone cancer.

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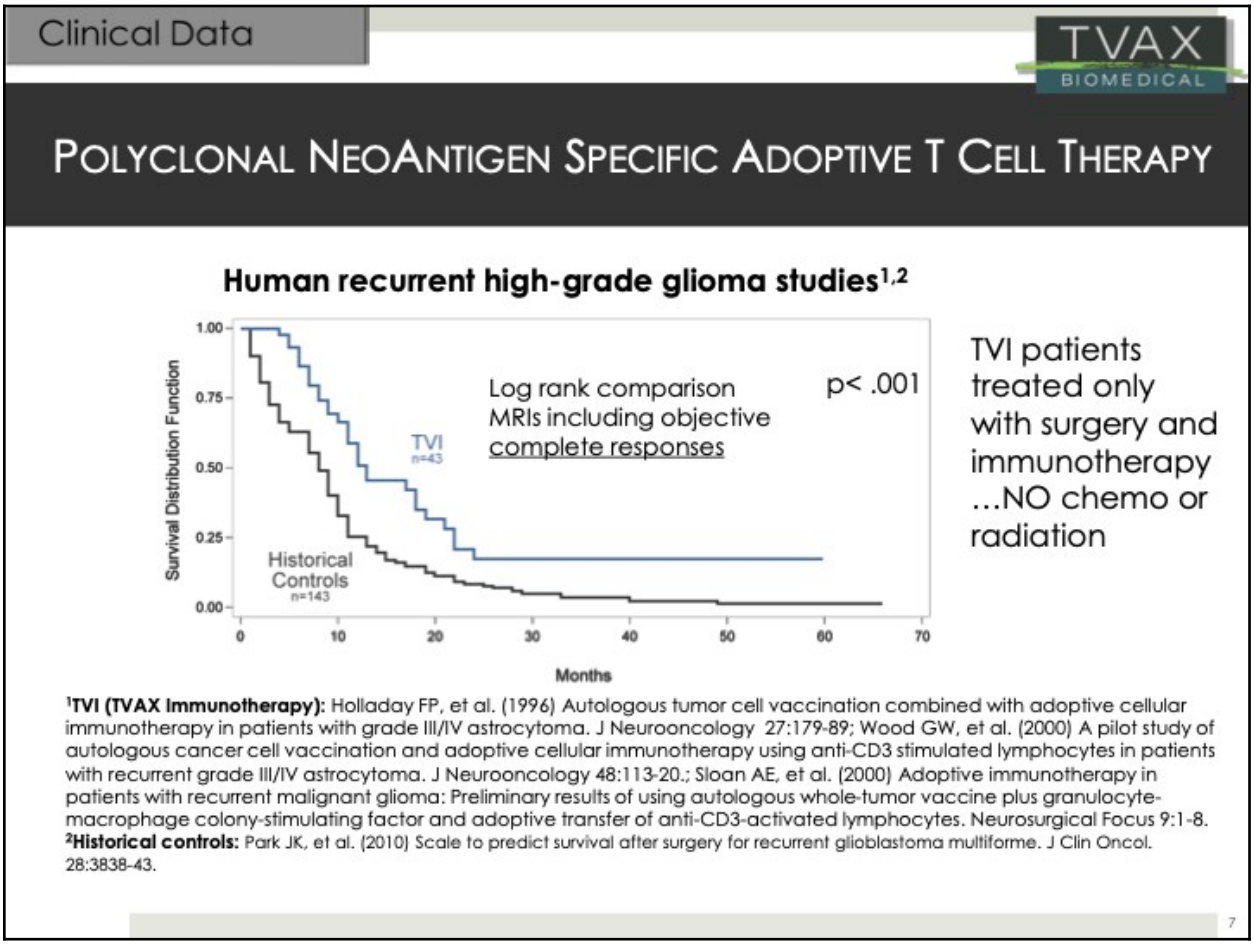
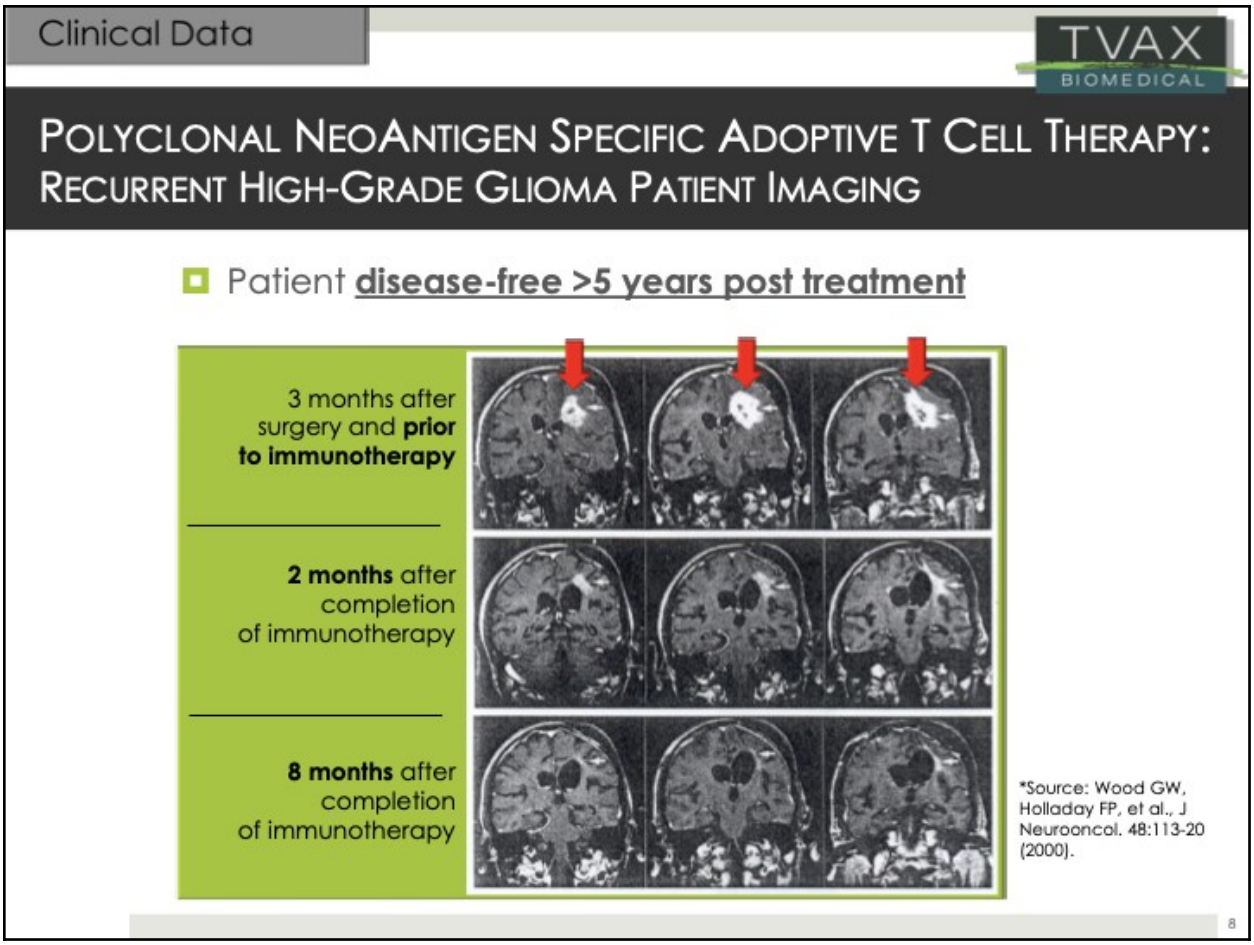
ELIAS is the company. They've gone on to complete their registration study. In January, this was approved by the USDA Center for Veterinary biologics for treatment of bone cancer in dogs.



Moving on to our human work, this is a Kaplan Meier curve that shows recurrent high grade glioma. We treated about 43 patients total with recurrent high-grade glioma. A total of 43 patients to-date have been treated with recurrent GBM. These are mostly stage IV. There were a few stage IIIs in here. The median survival is between about seven and eight months. If you look out at the 43 patients that we've treated, if you look just below the 50% function line, you can see we move survival out to about 17 months, which is good. The most important finding especially is at the bottom. About 20% of the patients went on to live five years or longer. So from a statistical perspective, obviously, it's statistically significant. It's important to appreciate that these patients were treated only with the surgery. This was the second surgery, at least after their GBM, and then the immunotherapy. There was no chemo or radiation therapy associated with this therapy at this point.

“A Unique Personalized Killer T-cell Treatment for Glioblastoma" (Wayne Carter, DVM, PhD) [#110]



This is one of the patients with a very large enhancing mass. This was three months after surgery and just prior to the start of the immunotherapy. Two months later, that mass has decreased significantly in size in these three slices. Eight months later, that mass is essentially completely gone, mainly just showing scar tissue which is remaining. This was a long term survivor that went on to live over five years and longer, then they were simply lost to follow up. In this situation those T cells were doing the work of a surgeon and debulking that tumor. We believe that the T cells are best designed to clean up minimal residual disease which is left behind after a surgery, rather than actually going in and debulking a surgery like they did here. That's why we've designed our current study the way we have.

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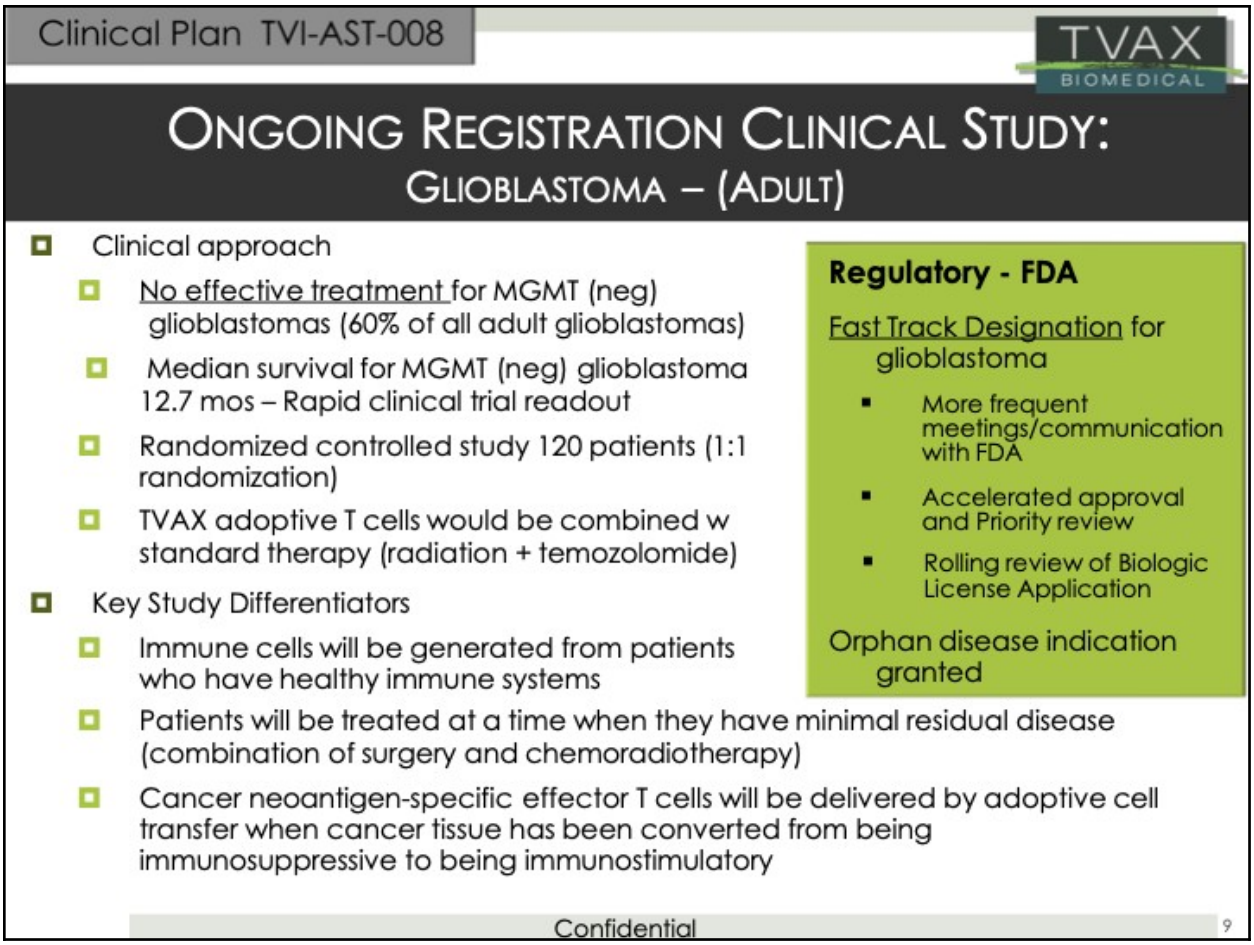

Our current study is focusing on newly diagnosed patients, and specifically MGMT (O6-Methylguanine-DNA-methyltransferase) negative. (MGMT defends normal cells against tumor initiation, however it can also protect tumor cells against the beneficial effects of chemotherapy.) These are the patients that do not respond to temozolomide (a chemotherapy drug used to treat certain types of brain tumors in adults). Their median survival is 12.7 months. Our patient population, our total patient study, will be a 120 patient study, one to one randomization, with the control group receiving radiation and temozolomide.

There are three key differentiators in this study, in comparison to what we've done in the past, that we think are going to differentiate this study in comparison to what I just showed you with the recurrent GBM.

- First of all, the immune cells are going to be generated in these patients while they have a healthy immune system. In the previous study, as you can imagine, the patients had very suppressed immune responses. They had received multiple rounds of radiation, chemotherapy, etc. These patients will have a naive, un-disrupted immune system, except for aging, but certainly not affected by chemotherapy or radiation therapy.

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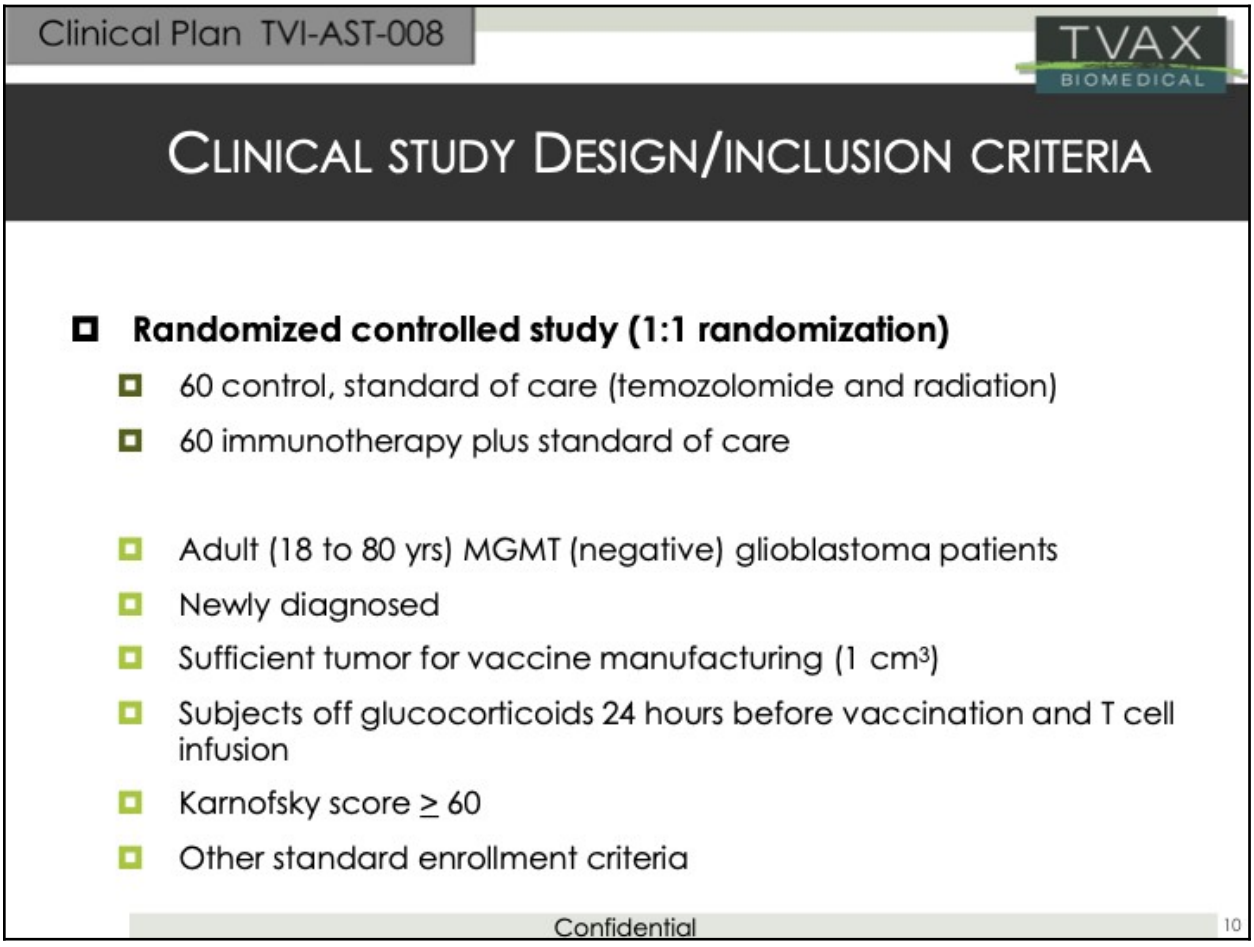
- These patients will also have minimal residual disease when they have the immunotherapy, and that's going to be brought about by the combination of the surgery and the chemo radiotherapy.
- Finally, the benefit of the chemo radiotherapy in this situation is it also converts an immunosuppressive microenvironment of the tumor into a more immuno-stimulatory environment, which is very favorable to the function of the T cells.

We believe that these three things are going to come together and bring about significant efficacy beyond what we've already seen before in the recurrent GBM setting.



This is a brief overview of the inclusion criteria. They are pretty standard. They have to be MGMT negative and newly diagnosed to qualify. We have to have sufficient tumor tissue to manufacture the vaccine. That's generally about a centimeter cubed. They have to be off of steroids.

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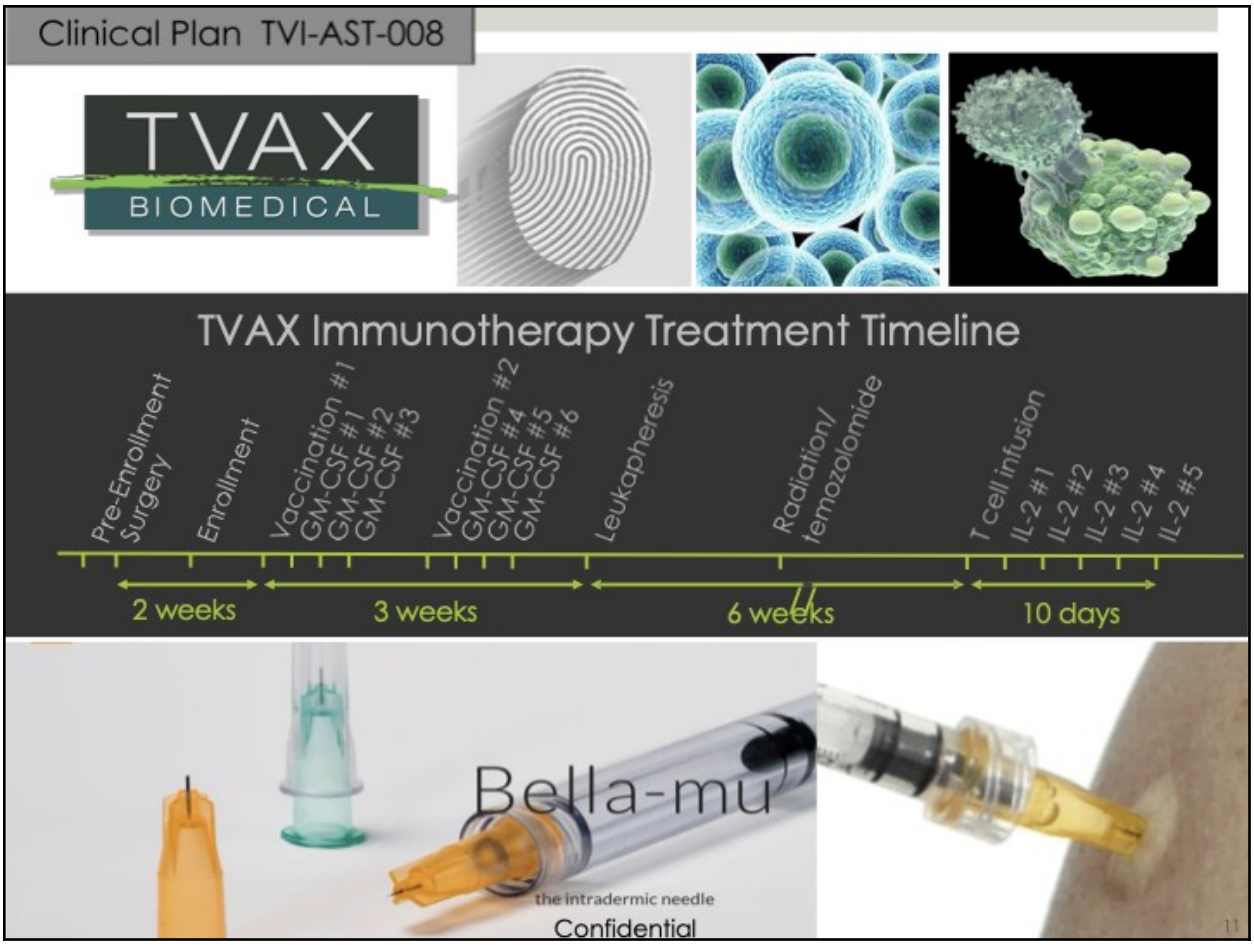

This is the way the timeline is set up:

1. We do pre-surgery informed consent. They sign the official informed consent after surgery, after we know for sure that they're a GBM and MGMT negative.
2. They then receive the first vaccination.
3. Then we continue to inject GM-CSF (Granulocyte-Macrophage Colony-Stimulating Factor, a kind of cytokine – a small protein important in signaling the body to produce white blood cells) as the adjuvant and to continue the dendritic cell activation directly into the vaccination site for the next three days.
4. Second vaccination, a week later.
5. More GM-CSF.
6. Then the leukapheresis (extraction of T cells).
7. It's at this point that we then do the standard of care, which is radiation and temozolomide.
8. Then after they're completed with that, after a six-week period of time, we give them back their healthy, activated effector T cells, and replenish their immune system.
9. Then follow that up with a low dose IL-2.

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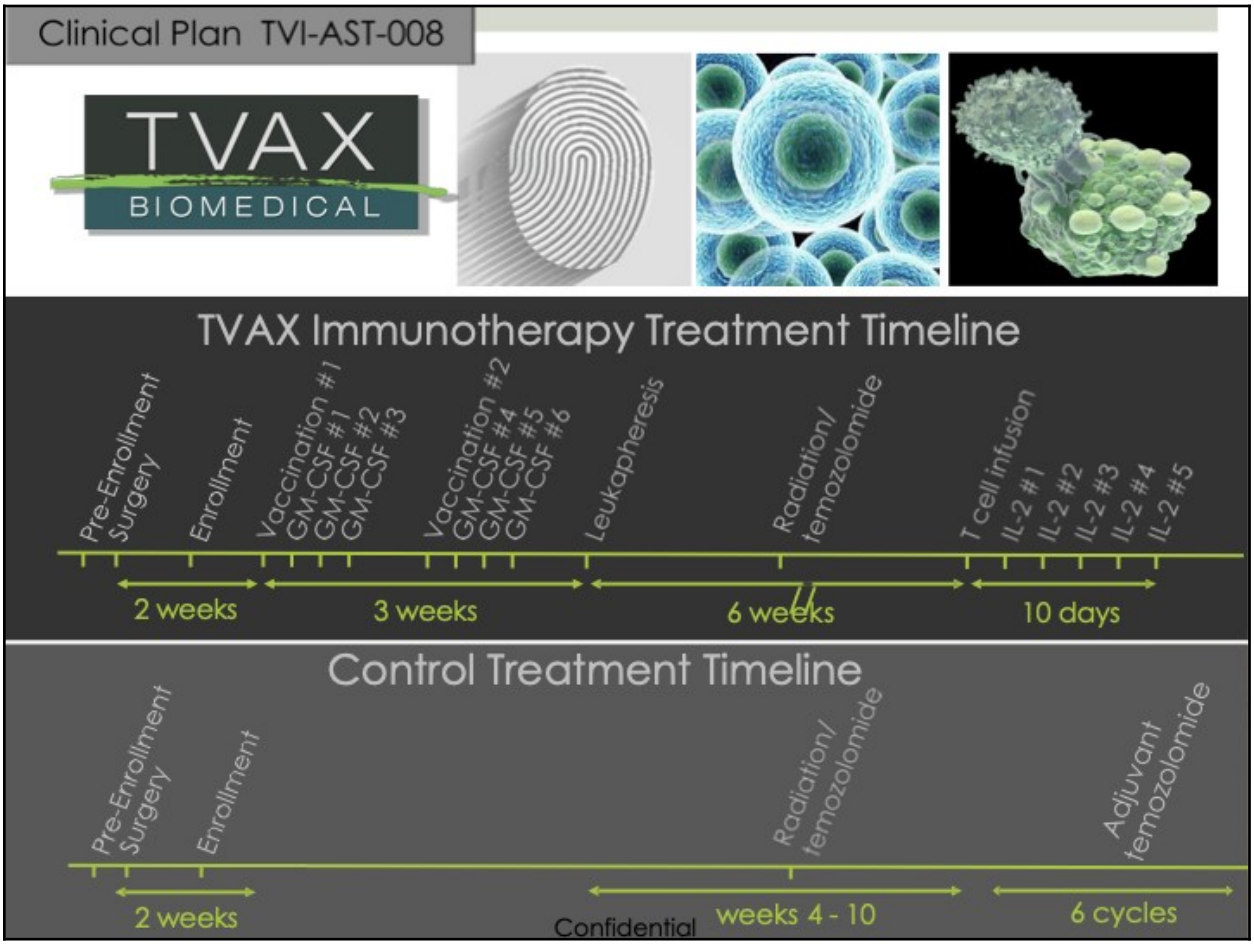
We're using a special needle for the intradermal vaccinations. It very easily facilitates intradermal vaccinations. You get a very nice response from the immune system intradermally, as opposed to “sub q” (subcutaneously) or “im” (intramuscularly).



Our control group looks essentially like this. The control group will receive adjuvant temozolomide. We know it really doesn't work in these patients because they're MGMT negative, but it is standard of care. So they will receive adjuvant temozolomide. The immunotherapy group will not because obviously that temozolomide would interfere significantly with the function of the T cells.

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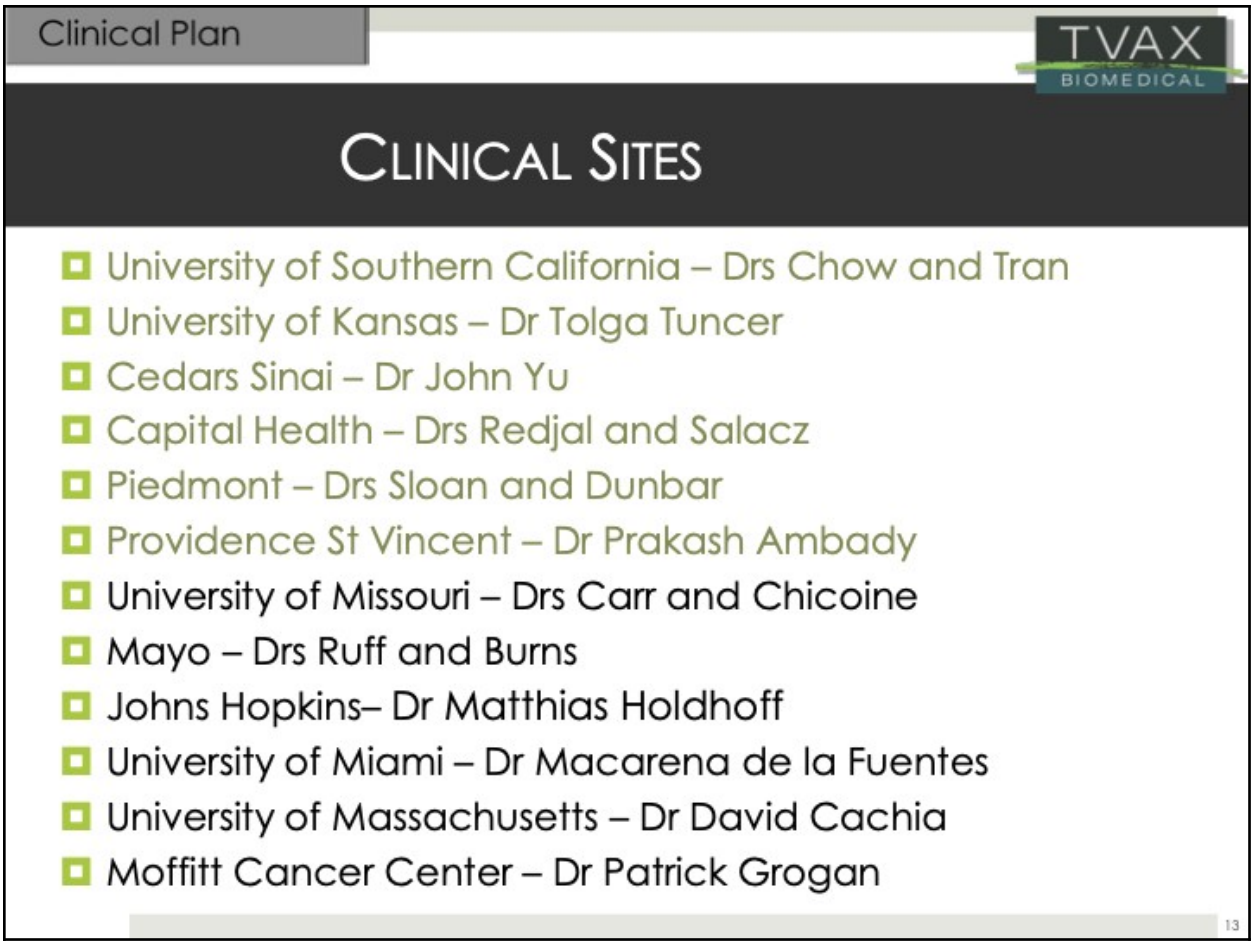

These are the sites that we have open: USC, University of Kansas, Cedars Sinai, Capital Health, Piedmont, and Providence. We're working on opening these additional sites and others beyond this.

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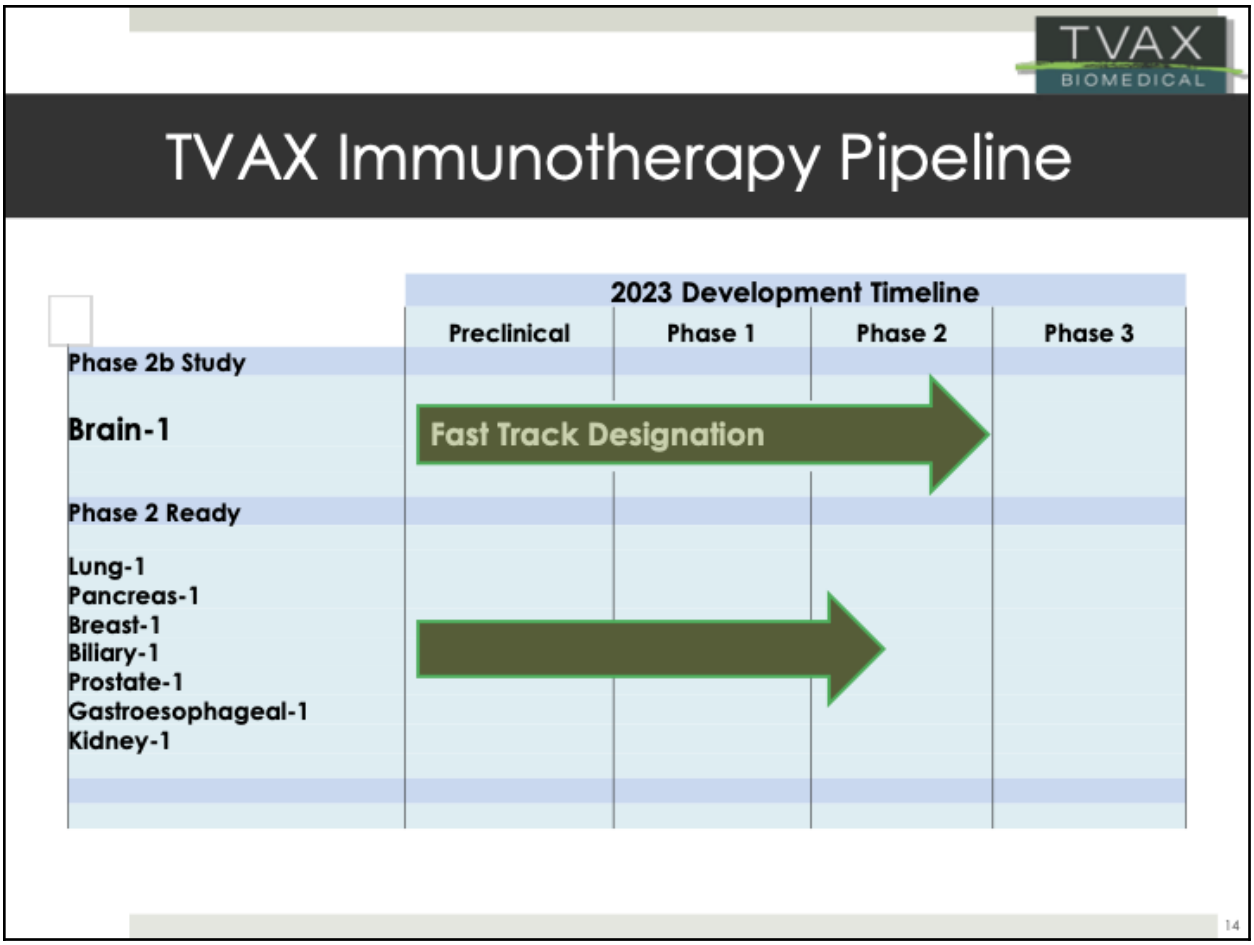

We're focused on GBM. It gives us our quickest path to an approval. We believe that this has potential for any cancer. Obviously, we need to have significant cancer tissue to develop the vaccine, but we believe that it has a potential to treat many different cancers, and certainly are very excited about trying this therapy in other cancers in the future.

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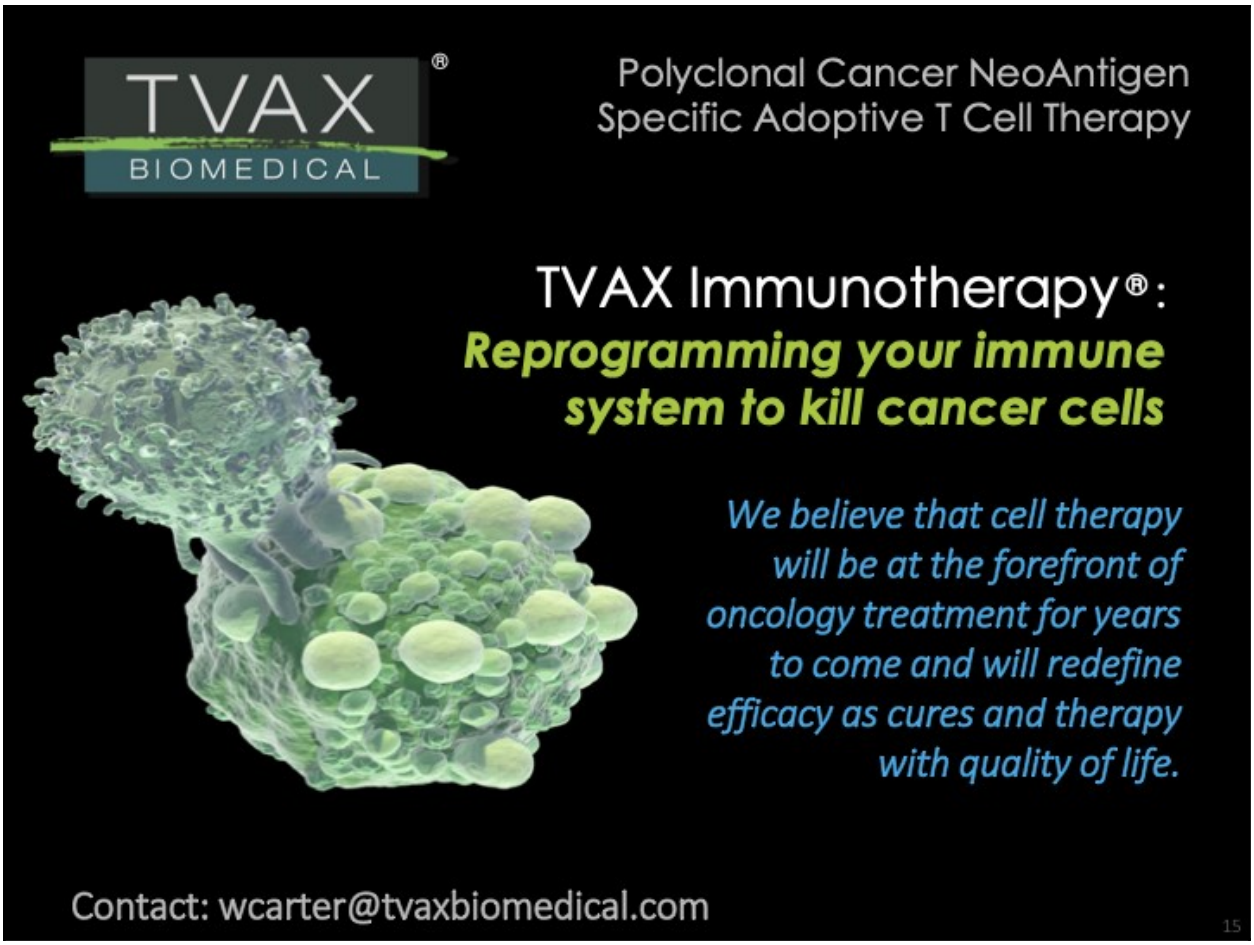

Brad Power 14:38
There are a lot of choices in that timeline that you laid out: the adjuvant therapy, when you do this and when you do that. When I had my chemo, it was five rounds at three weeks apart, or it could be six rounds at two weeks apart. There are a lot of variables in there. You've got both which elements you have in that treatment regimen, and then the respective timing. How have you arrived at that, because there were a lot of choices embedded in that?

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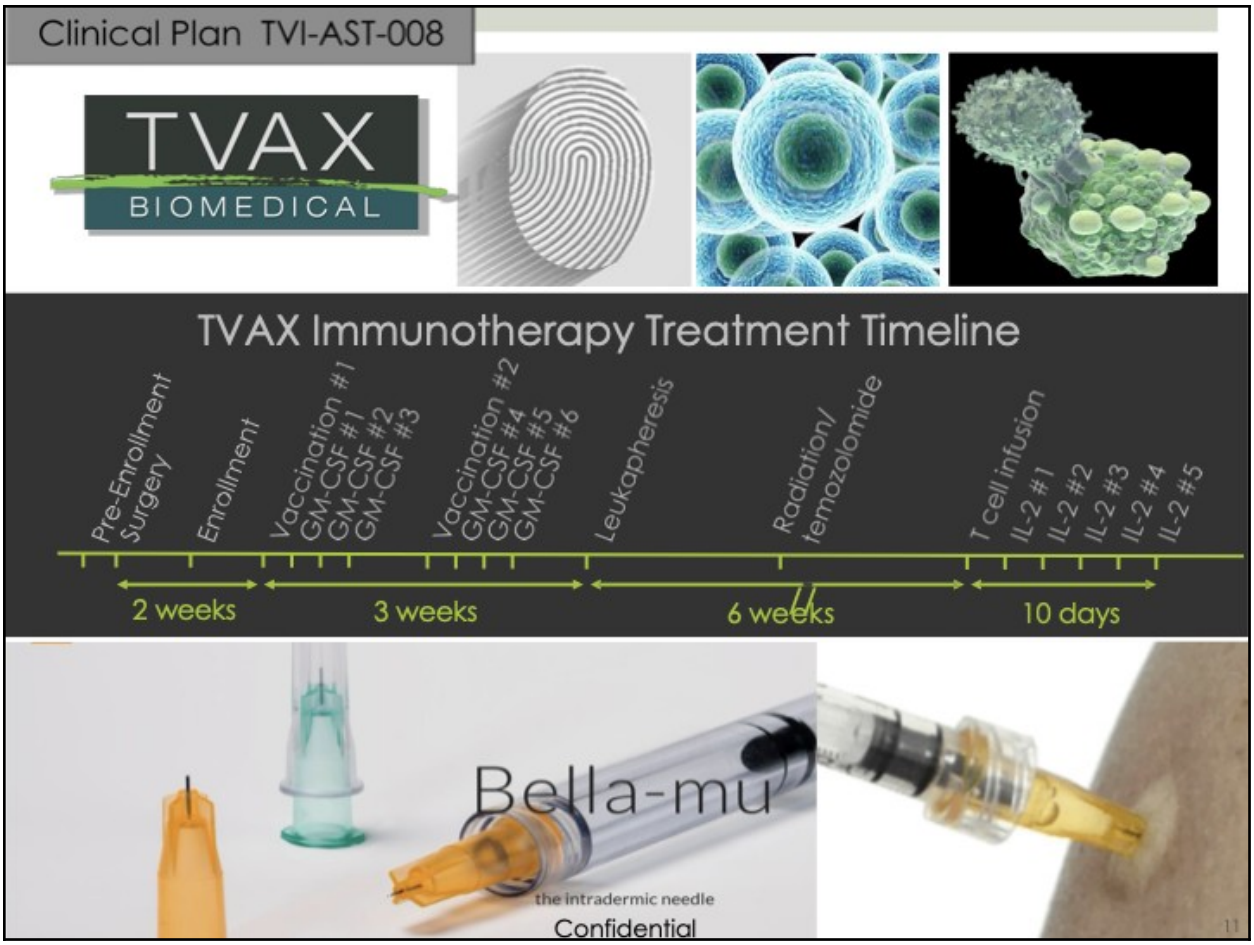

Wayne Carter 15:23
We worked with many different experts in the design of this; especially neurosurgeons and neuro-oncologists with the recurrent GBM. We were working a lot with Dr Andy Sloan and also Dr, Mike Salacz and Dr Paul Camarata. We certainly had good efficacy, but we recognized that we were fighting this issue of, how can we treat patients when their immune system is as healthy as possible? Because that's what we're relying on here. We are relying on the patient's own immune system to treat their cancer. We have designed this and designed all of the vaccination and the collection of those T cells up front before the patient ever receives chemotherapy or radiation therapy, because it does have a significant detrimental effect on the function of your immune system, just as steroids do. These patients are all on steroids after the surgery because you need to reduce the brain swelling. But we are very careful to make sure that they're off those steroids before they can go on to the vaccination protocol, and the same with the T cell infusion. They've got to be off of steroids before they receive the T cells. Because we know that those steroids can have a negative effect on the T cells, and we want to make sure that the T cells have their best opportunity as possible to identify and then kill the cancer cells.

Brad Power 17:20

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Could you speak to the last section there, the IL-2? It happens that I just had leukapheresis. I could show you the catheter hole in my neck, and I'm going to be getting CAR-T in the middle of October, but it will not have an adjuvant like an IL-2. How did you arrive at that? And what's the significance of that?

Wayne Carter 17:41
It's derived from experts that we've been in consultation with. It is a low dose IL-2. First of all, you don't have the clinical side effects that you have with it, but you do get the continued expansion of your T cells in vivo. That's why we're giving it, giving it in a low dose, basically every other day, for a total of 10 days. It's to continue that in vivo expansion of your T cells.

There are some T cell therapies, and I believe TIL therapy does generally recommend IL-2, just as we are.

Robb Owen 18:32
I'm here as eyes and ears for a friend of mine whose husband has glioblastoma. He had his initial surgery in December of last year, and has been trying multiple different avenues with marginal success. That would eliminate him from something along these lines, based on this tumor already being excised?

Wayne Carter 18:55
That is correct. We have treated emergency authorization use patients. That could be a possibility for him down the road, but we have to have at least a centimeter cubed of tissue.

Robb Owen 19:09
There has been some recent growth with it, but I'm not sure whether another surgery would be advisable.

Wayne Carter 19:27
I'm an immunologist. I'm a veterinarian by training, but also an immunologist. It does just make so much sense. We're educating your immune system so it recognizes your own tumor, and then it can eliminate it.

Robb Owen 19:50
I work on the front end of that by using nutrition and supplements to build the immune system. Something like what I'm working on put together with what you’re working on could be remarkably successful.

Wayne Carter 20:01
I couldn't agree more. You are what you eat, and so much of our diets are contributing to our cancer and predilections and so forth, and so that is an extremely critical aspect of therapy and maintaining a healthy immune system and maintaining an immune system that's able to eliminate your cancer.

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Gitte Pedersen 20:34
Amazing results. That’s a very hard cancer to treat.

Are you using the T cell response to select the neoantigen, or are you analyzing the neoantigen to select the T cell?

Wayne Carter 21:00
That's a very good question. A lot of institutional investors and others will say, “Well, why aren't you selecting for this antigen or that antigen, or these five antigens?” The bottom line is, every tumor is different. If you go back to the name of the treatment that I started, it's “polyclonal”. We don't care what the antigens are. We basically take all of the antigens which are presented on that cancer cell and develop them into a vaccine. Then you're vaccinated against all of the antigens which are present on those cancer cells. Your T cells are then being primed against all of the antigens. We're not selecting for specific antigens and then focusing on T cells that are responsive only to those antigens. We are literally creating a polyclonal response with the vaccination, and then with the T cells also.

Gitte Pedersen 22:06
The way you're doing that is taking the tumor tissue, mincing it, and exposing the T cells that you harvested?

Wayne Carter 22:24
The cancer tissue is minced and degraded. Our goal is to end up with a single cell suspension. We know that the intact live cells are better recognized by the immune system. We use the whole cell that's been attenuated with 50 gray of radiation and then combined with the adjuvant. It's the whole cell generally, which is what we're aiming for to then vaccinate the patient against.

Gitte Pedersen 22:58
After the alephoresis, the patient gets the T cells and the minced tumor cells reinjected with an adjuvant.

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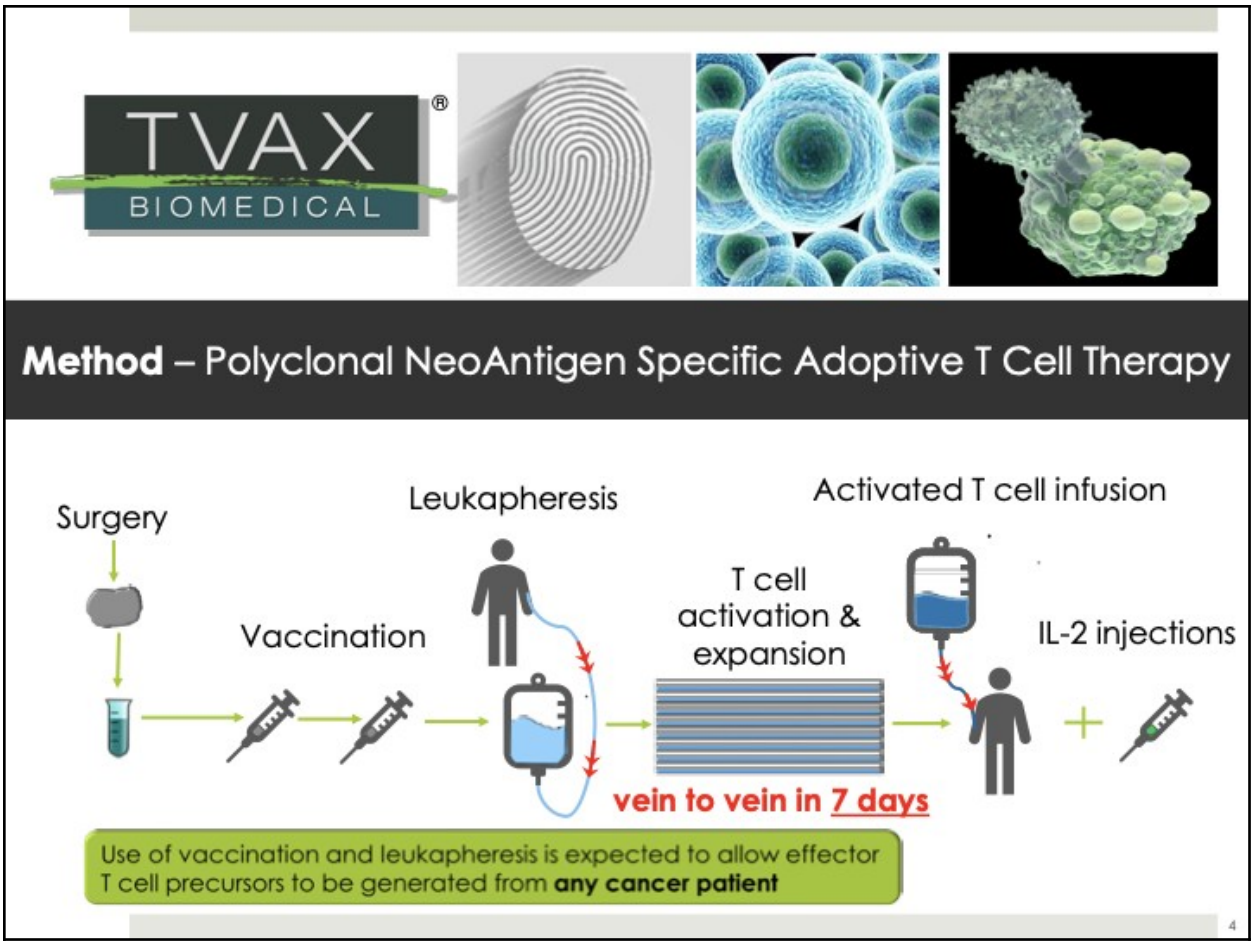

Wayne Carter 23:21
Going back to the slide I covered before, the surgeon removes the tumor, and then that tumor gets sent to our manufacturing facility. We use a combination of mechanical and enzymatic digestion of the tumor so that we end up with a single cell suspension. Our minimum number of cells that we need is generally 50 million. It's those 50 million cells or more which are then attenuated with 50 gray of radiation. Then we combine that with GM-CSF as an adjuvant, and then the patient gets vaccinated against their own cancer live cells, but they're attenuated, so they're no longer capable of growth. When we inject them as a vaccine, they're not going to grow, but the immune system picks them up, recognizes that they're foreign, and then develops T cells, which are now primed against those antigens which are present on the tumor cell.

Gitte Pedersen 24:25
I may want to make an introduction to a company that is also enhancing vaccines. It's more like an individualized adjuvant. That's probably the best way to put it.

You just need tumor tissue in order to do it correctly. We have to teach all the treating physicians out there to store some at some point, because it seems to be a limiting factor in a lot of the work here.

Brad Power 25:12
I don't know if you just said this, but is that fresh tissue then, and does it need to get to your lab within 24 hours, that kind of thing?

Wayne Carter 25:21
Yes. Correct. We need fresh tissue, and generally we receive it within 24 to 48 hours, shipped on wet ice, four degrees centigrade. It takes us about 48 hours to turn the vaccine around. We can manufacture the vaccine pretty quickly, and then we just store it at minus 80 before it's ready to be administered.

Richard Anders 25:49
What do you think you'll be charging for this when it goes to market?

Wayne Carter 25:58
It's a little early to say definitively, but I can tell you that we think we're going to come in significantly under the price of the existing CAR-Ts and TIL therapies. CAR-Ts right now are between $350,00 and $430,000 per treatment. TIL treatment, the last I heard, I think they're aiming for $515,000 per treatment. We are planning to come in less than either of those. We think we're going to be extremely competitive and comparable in cost, even to some of the other PD-1, PDL-1 inhibitors, which can be as much as $200,000 per year, and you have to be on continuously. This is a single treatment. We believe that we'll be able to price very competitively, and part of our reasoning behind this is we believe that this therapy should ultimately be available to a lot of people, and we think pricing in this range will make it available ultimately to a lot of people.

Richard Anders 27:11
Your cost of goods won't be that high?

Wayne Carter 27:14
There are significant cost of goods when you have to think about this kind of GMP (Good Manufacturing Practice, a set of principles and procedures that ensure the quality of products during the manufacturing process in the production of pharmaceuticals) manufacturing, but there certainly is plenty of space for profitability of the company and yet also developing something that we think is very reasonable for payers to consider.

Richard Anders 27:34
A question about adverse events: you're doing significant immune stimulation with all sorts of cells. Are you seeing any autoimmune disease manifestations in your patients?

Wayne Carter 27:51
We've never seen any autoimmune manifestations at all. Again, these are your own T cells. They're just T cells which have been primed against your cancer. There's really no reason why there should be any autoimmune activation, and we haven't seen any. About a third of the patients will have sort of a low grade flu-like symptom when they get their T cells back. And

that's about it. That's really just a manifestation, primarily, of these T cells producing TNF alpha (Tumor Necrosis Factor alpha, a protein that's a key part of the immune system and is involved in many inflammatory processes). The patients are getting a little bit of TNF alpha when they get their T cells back. They'll get, sometimes, a low grade fever, a little bit of malaise for 24 to 48 hours. And that's really about it.

Richard Anders 28:35
You're injecting cancer cells, but they're not just cancer cells.

Wayne Carter 28:45
That's where the immune system works with the HLA proteins and so forth. (Human Leukocyte Antigens are proteins that help the body's immune system identify foreign invaders and distinguish between the body's own cells and tissues.) So you recognize self, and once you recognize self, then you don't develop an immune response against it. We haven't seen any autoimmune.

Richard Anders 29:01
It looks like you were a one-to-one randomized clinical trial. I'm wondering why you didn't do a two-for-one or something. The effects of glioblastoma are so incredibly severe, you'd get signal with the two-for-one randomization, or probably a three-for-one, and you would get more patients in the trial.

Wayne Carter 29:28
We've had that discussion with the FDA, with investigators, and there have been, as you can imagine, a lot of different opinions about the right way to do it. Ultimately, we sided with the FDA.

Richard Anders 29:48
The FDA wanted one-for-one?

Wayne Carter 29:49
Yes.

Richard Anders 29:52
I imagine patients would have loved two-for-one or three-for-one.

Wayne Carter 29:54
Absolutely. We also considered a synthetic control arm, all sorts of things, but right now we're just focused on one-to-one.

Richard Anders 30:04
It's not hard to recruit?

Wayne Carter 30:07

Well, it's been slow. There's no doubt about it. Our recruitment is slower than what I want, but we're moving forward.

Brad Power 30:23
Bill Paseman in the chat noted that your paper lists 2000 as the image date. How long have you been doing this?

Wayne Carter 30:36
That's honestly the biggest frustration, I'd say, that the company has had. Quite honestly, the founder of this technology, Gary Wood, I would say was well ahead of his time. (Gary W. Wood, Ph.D., founded TVAX Biomedical in 2004 and currently serves as Chief Scientific Officer and Chairman of the Board of Directors.) He developed this technology and started treating patients in the 1990s, and some of the recurrent patients that were on that graph were treated back in the 1990s. The company was actually founded in 2006, and by the time the company was founded, immunotherapy PD-1, PDL-1 inhibitors were beginning to take off. Nobody was interested in T cell therapies, or cell therapies in general, and it really wasn't until CAR-Ts were approved that there began to really be a significant interest in funding T-cell therapies. We struggled so much with funding on the human side that in 2012 the company tried to do an IPO, and there simply wasn't the support. And so pulled back, and that's when we shifted to animal health. Kansas City is known as the Animal Health Corridor of the world. We were able to get investors to develop it on the animal health side. We now have an approval for dogs to treat bone cancer way ahead of treating anything in humans. It's simply because the funding wasn't there, and that is the reality of the technology and the funding environment. Now, we've been able to get the FDA fast track. We have an FDA grant. We have investors that are interested in moving this forward now, and so it is certainly a different environment. It's still a challenge. It's still a significant challenge to raise the money that's needed to do this study. But it simply was all an issue of funding, and the marketplace not being ready to fund a T cell therapy.

Brad Power 32:50
Picking up on your comment about immune checkpoint inhibitors. Roger Royce asked in the chat: Do you combine this vaccine with checkpoint inhibitors? I guess not, because you didn't list it. But have you considered it?

Wayne Carter 33:02
We've absolutely considered it. There are a lot of things which are very logical. Certainly that is one of the things. You certainly could bind the vaccination with a checkpoint inhibitor. You certainly could use the checkpoint inhibitor after you receive your T cells back. So I think both are very good suggestions.

The other thing, and I didn't mention it in our slides, we have a joint venture with another company called Genelux, and they offer an oncolytic virus. We believe that there's a great synergistic opportunity between an oncolytic virus and our therapy, because the oncolytic virus in its action will create inflammation in the lysis of that tumor cell and bring in other inflammatory

cells. We think there's a great opportunity for synergy between an oncolytic virus and our therapy. We were granted a patent specifically to give us that opportunity.

Mark Stoner 34:03
Like Brad, I have diffuse B cell lymphoma. I start CAR-T treatment September 2, bridging technologies, next week.

What's the difference between a T cell and B cell? And also, is the B cell a separate expansion for you, or apples to oranges?

Wayne Carter 34:23
They're completely different immune cells. Your B cells are a cell which is producing antibodies, your T cells are a cell which provides long term immunologic memory to your immune system. They both provide that long term immunologic memory, but B cells do it through the production of antibodies, and T cells simply through their ability to either directly kill another cell or bring in other other cells into that inflammatory milieu. They are very different cells.

We are only focused on T cells, and using T cells, ultimately to kill the cancer cell. We have generally learned through many years of immunology research, that it's really not your B cells that produce cancer immunity. The cells which are really important to be able to fight and potentially cure cancer are your T cells and not a B cell.

Brad Power 35:34
Okay, picking up a couple more questions from the chat, Allen Morris, who's a pathologist and an advanced prostate cancer patient asks: Have you ever heard of the concept of antigen competition? And if so, what is your notion of it?

Wayne Carter 35:51
You mean as it, as it relates to what we're doing in this situation? I guess I'm a little bit lost as far as exactly the purpose of the question.

Brad Power 36:02
You were talking about it being polyclonal. I guess polyclonal means there are multiple antigens that could be stimulating things. Could they be competing amongst themselves?

Wayne Carter 36:15
There's always that possibility. My bias would be that I rely on our innate immune system, to be able to figure that out. Maybe Dr Morris is going to provide more insight there on that question. Our immune system has the ability to develop those appropriate responses to individual antigens and then figure out the appropriate responsiveness there. When we try to engineer something too much, sometimes we're successful at doing that, and sometimes, we can interfere with the proper function of a system.

Allen Morris 37:15

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Antigen competition is a profound concept, and I believe it's not on the radar screen of any vaccine person.

Another concept in the basic science of molecular biology is T cell hierarchies.

Do you believe what you're doing is a non-selective way of trying to punch through that or is your process not going to be active at punching through that?

Wayne Carter 38:07
I think it will. We'll be able to overcome potential hierarchical issues that may exist within T cells. There's so much that we still have yet to learn. To some degree, we're still in our infancy. One of the things that I like about this technology is that we are relying on the immune system itself to be able to figure out how to overcome these issues of the myriad of different T regulatory issues that the cancer cells, the cancer environment, the micro environment, throws at the body. This is one way in which we're able to overcome that. Some of this is mass action. There's an opportunity to combine this therapy with other therapies, as we mentioned, the checkpoint inhibitors and others. This is not going to be the panacea treatment for everything. A combination therapy always tends to work better. If you put two or three different therapies together, they tend to work better than a single one alone. But I do think that this T cell approach is moving in the right direction to get your own immune system to fight your cancer.

Brad Power 39:46
There's a question here from Martin Luzbetak in the chat: Do you ever have a problem getting enough T cells through the apheresis?

Wayne Carter 39:57
We have not. We generally do two leukaphereses, but we have never had a problem of not having enough T cells. As I mentioned our vein to vein time is seven days. We could expand that expansion time in the lab. We don't need to. Within that seven day period of time we're able to activate the cells and have a large number of T cells that we then administer back to the patient. We have not reached a toxicity level on administering the T cells.

There are many ways this therapy can be potentially expanded. We've already talked about adding the PD-1, PDL-1 inhibitors. We could potentially add in additional doses of T cells down the road. There are many ways that this therapy could potentially be expanded. Our focus right now is just to get it approved, and then begin to turn over to the hands of different oncologists to try to figure out other ways to expand it. But our goal right now is laser focused on an approval.

Brad Power 41:18
Roger Royce asks a question in the chat: how often do you get an immune response from the vaccine? Is it 100%?

To add a little color to this, I know Roger has gotten a personalized vaccine recently, and he just told me today that he got an ELISpot test (Enzyme-Linked Immunosorbent spot, a highly

sensitive immunoassay that measure the frequency of antigen-specific T cells by measuring the number of cytokine-secreting cells within the blood at a single cell level).

It raises a question: are there companion diagnostics that you can use through this process that are measuring the effectiveness of your vaccine?

Wayne Carter 41:46
That's a good question. We use the DTH response, the Delayed Type Hypersensitivity response, (the recruitment of T cells into tissues to be activated by antigen-presenting cells to produce cytokines that mediate local inflammation), which is the like the tuberculin test when you get a TB test. After the first vaccine, we generally have about 90% of the patients demonstrating a positive DTH response. After your second vaccine, it's essentially 100%, and that's across a myriad of different types of tumors. There are some people that suggest that some tumors are more immunogenic than others. We have not found that. We have seen a positive immune response against any tumors.

Brad Power 42:27
That is very encouraging, given that there are a lot of cold, solid tumors that don't have immunotherapy working.

Brian McCloskey 42:38
Do you do any pre- or post-immune profiling of the patients?

Wayne Carter 42:46
Pre, no. The only inclusion criteria for these patients in our study are their lymphocyte count. We want a lymphocyte count of at least 800. Other than that, no, we're not doing any specific immune profiling to look at specific T cell populations or anything like that. We certainly do that post hoc. We have a variety of different biomarker studies that we're going to be running as part of this, but not as inclusion criteria.

Brian McCloskey 43:21
What I'm trying to get is just understanding who's going to respond and who's not going to respond. If you get a better profile, you're going to understand who's a good candidate.

Wayne Carter 43:31
I completely agree. We're laser focused on getting an approval. As part of the study, we are collecting all sorts of different samples which will be used for immunophenotyping, for genomic analysis, for proteomic analysis. We have a large number of different biomarker collections which are being done and which will be analyzed specifically to look at why some patients are responding and others are not

Brad Power 44:09
Vanessa Hugo, I don't know if you mind me putting you on the spot, but I would really like to get a perspective of a brain cancer patient. You're the caregiver to your husband, Michael. Al

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Musella walked us through 10 different possible therapies that he would recommend people consider. I assume this is on the list. How do you rate this amongst the other treatment options that you and Michael are considering?

Roger Royse 45:35
My perspective as a patient is I'm just kind of blown away looking at this, because you've got this down to such a clear and fast process, because it took me a good six months to get through this here. I did something similar to this here and in Japan. It took about six weeks, because they don't have an FDA, but still, the seven days, vein to vein and and I think you said six weeks to actually get the vaccine manufactured.

Wayne Carter 46:06
48 hours, two days.

Roger Royse 46:09
That's pretty amazing, because I had a neoantigen peptide vaccine. I also had NK and dendritic cell expansion at the same time, and some other things through the Jaime Leandro Foundation. With the JLF, with our vaccine, just the time people sat around waiting. About half the patients died waiting for the design and testing to be completed. So that's a big deal if you can get this to the patient that quickly,

Wayne Carter 46:42
A lot of those vaccines are being developed off of genomic sequences. That's where all of the time gets added in. Our issue is we've got to have fresh tissue, and we need about a centimeter cubed. Those are the limitations. But assuming that we can have that fresh tissue and enough to be able to harvest at least 50 million cells, then we're good to go.

Brad Power 47:19
Vanessa had a response in the chat which you may want to respond to. She's very knowledgeable about all of the possible therapies, and she says this is a great therapy candidate, just limited access due to the pre-surgery trial enrollment requirement, that fresh tissue, and not having been on other treatments.

She would love to see this combined with Optune (a wearable device that uses adhesive patches to deliver continuous therapy to the area of your brain where your GBM tumor is located), plus maybe a checkpoint inhibitor.

Wayne Carter 47:48
We've had some neurosurgeons that have been interested in potentially adding this to Optune. From an FDA perspective, it needs to be as clean as possible. We're certainly interested in potentially doing something like that down the road, just as we would be with a PD-1, PDL-1 inhibitor. Right now, we're focused on the approval.

If somebody wanted to participate as an experimental use patient, and wanted to use Optune in addition to this, and they had a PI (Principal Investigator, a researcher) that was willing to function for them as their investigator then we're happy to entertain possibilities there. Our study needs to be clean for the FDA.

Chris Apfel 48:48
Congratulations on this very impressive technology that you have developed and worked on for so long. As an entrepreneur myself, I know how long it takes to get to market adoption, and so congratulations to this tenacity and sticking with it. I think it's very clear that everybody who is here on the call is very impressed with what you and TVAX and the founders have built there.

I have one technical question, and that is in regards to the vaccination. It looks to me like after you have isolated the tumor cells, after the surgery, they are injected twice. The question is, why twice?

The other question is, you said “at least 50 million cells”. Do you really? Do you know? How do you know how many cells to inject? Because you also don't want to induce any T cell exhaustion, and so I am concerned that you may actually even overwhelm the immune system and the T cells so that you may not have enough selectivity for the T cell activation and expansion.

The second question is, with the vaccination, you hope that you actually have these T cells, and they can be polyclonal, because the antigens and even the tumor itself may be heterogeneous. You would hope you have a higher proportion of T cells that are directed against the tumor, but it does seem like the T cell activation expansion is not during the activation and expansion. Are you exposing these T cells also to the primary cancer cells as well? This is the technical question.

Wayne Carter 50:46
I'm going to focus on the last question first. You're asking if we're using the cancer cells as part of the activation. We are not. We're using anti-CD3 (Cluster of Differentiation 3, a protein complex and T cell co-receptor that is involved in activating both the cytotoxic T cells – CD8+ naive T cells – and T helper cells – CD4+ naive T cells).

Chris Apfel 51:02
Why is that?

Wayne Carter 51:05
Because you get a pan response to activate the cells. You get a much stronger response than you get when you use any antigen, like a cancer antigen. We get a more robust response and a more reproducible response by using anti-CD3. So that's what we use.

Chris Apfel 51:24

Then the first question is, selectivity with the vaccination. How do you know that you're not overwhelming the immune system?

Wayne Carter 51:35
I don't believe that we are. We're getting a good immune response. I know that in some of the early studies from my founder, he did quite a bit of work trying to identify the right number of cells to ultimately come up with that vaccination number that we have. We vaccinate the patient in four different locations, two in the axillary (armpit) area, two in the inguinal (groin) area, just to cover a large number of lymphatic drainage and lymph node locations. Then they receive that vaccination again, twice. In some situations in the past, we've done three vaccinations and have found no significant difference there. We have backed off to just doing the two vaccinations at this point.

Chris Apfel 52:28
If I had a glioblastoma, and I wanted to have it today, could I get access according to the Right to Try act? Is it possible to get your treatment outside of the study?

Wayne Carter 52:56
It would be possible. We would qualify you just as an emergency use authorization patient. That would be a possibility.

Chris Apfel 53:10
I don't know whether enrollment is difficult. In my mind, enrollment should be very easy, even if it's one-to-one. From the total number of patients, you need to show a statistical difference. The one-to-one is the ideal randomization proportion so that you'll get with a minimal number of patients to have basically the maximum power in proportion to the number of patients exposed or participating in the trial.

I don't know whether the randomization is a barrier for your recruitment?

Wayne Carter 53:51
It’s not. There have been a variety of issues. One of the things that we recognize is that most of these patients come in through the emergency department. We have to have fresh tissue. If a surgeon cuts on a patient before they recognize that there's a clinical study ongoing, if, let's say the neuro-oncologist is the PI and hasn't adequately communicated with a neurosurgeon, then we could lose a patient there. We've lost some patients because they just have done so poorly after the craniotomy that they've gone right into hospice. We have lost patients because they're MGMT positive. Like any clinical study, they always take longer than you want them to. I'm with you, I just can't imagine why we're not blasting through our enrollment. But the bottom line is, it's tough. That's why we have six sites open, and it's why we're going to be opening at least another six or nine sites over the next six months, because we need more sites. We need more neurosurgeons, and unfortunately, we need patients, but we also want to find a solution for them.

Chris Apfel 55:12
The Kaplan-Meier curves there were really impressive. A five year long term survival of benefits of at least 15%, almost 20%, that's what it looked like on the Kaplan-Meier curve, is very impressive. What about the other 75% or 80%? It can't be just the immunosuppression through the temozolomide. Do you believe that some of them may just not be accessible through this immunological approach?

Wayne Carter 55:44
We showed a benefit to pretty much everybody. That whole Kaplan-Meier curve was shifted to the right, and so there was a benefit in a large number of those patients. But it is important to appreciate that we are relying on the patient's immune system to fight the cancer. And so those patients, a lot of them are older. In this situation, they were recurrent, so they'd had multiple craniotomies. They had had radiation and chemotherapy to suppress their immune system. They had many doses of steroids. They had so many things going against their immune systems. And yet, that's exactly what we need to fight the cancer.

It is the reality also of where we are today in our treatment of cancer. We give all of these therapies that have this negative impact on the immune system, when the one thing that your body has to potentially fight the cancer itself is your immune system. In the future, in years and decades to come, we're going to realize that the more we can maintain the integrity of the immune system, the better off that patients are going to be, as far as being able to fight their own cancer.

Brad Power 57:02
From Martin Luzbetak in the chat: What is the dose of IL-2?

Wayne Carter 57:13
I don't want to misquote, but I'm happy to reply. They can email me, and I'm happy to give the dose. It is a low dose,

Brad Power 57:23
Ryan Moon asks: I know you mentioned glioblastoma, but I was wondering if you're working with any other grade IV gliomas, namely, diffuse intrinsic pontine glioma?

Wayne Carter 57:36
We are not, but we have intentions to look at a large number of cancers, assuming you're able to get this approved or have significant funding. We'd love to refocus this again on recurrent. There are so many patients with recurrent GBM that we'd love to go after recurrent GBM. But, certainly MGMT positive. You can go down the list. These patients need a therapy that works for them, and so we are very anxious to try to move into other other tumor types.

Brad Power 58:11
Bill Paseman asks: What would you need to do to treat kidney cancer?

“A Unique Personalized Killer T-cell Treatment for Glioblastoma" (Wayne Carter, DVM, PhD) [#110]

Wayne Carter 58:17
When we first did our kidney cancer study, we had a very nice improvement in survival in those patients, and that was before the checkpoint inhibitors were approved. Today it would make a lot of sense to combine our therapy with a checkpoint inhibitor and look at the benefit. That would be my approach.

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CHAT COMMENTS

00:26:50 Gitte Pedersen: Questions 1) How do you select the most effective neoantigen in the specific patients and how do you use that to select the right T cells to expand ?
00:31:05 Gitte Pedersen: 2) What is the reason that this works - do you have any vaccine adjuvant
00:32:37 Bill Paseman: I noted that the paper lists 2000 on the image date. How long have you been doing this?
00:41:43 Roger Royse: Do you combine the vaccine with checkpoint inhibitors?
00:48:40 allen morris: Have you ever heard of the concept of antigen competition? And if so, what is your notion of it?
00:49:06 Martin Luzbetak: how often do U fail to Apherese enough of Tcells?
00:49:48 allen morris: Have you ever heard of T cell hierarchies and if so what is your notion of it?
00:52:02 allen morris: Do you know of any successful T cell delivery platforms other than adoptive cell transfer?
00:53:21 Roger Royse: How often do you get an immune response from the vaccine? Is it 100%?
00:56:02 Roger Royse: Allen - this ties into your prior question about hyper progression because there is a "theory" that activating some T cells might crowd out (in my layman's terms) other immune cells that may have been controlling the cancer. My docs told me that this rarely happens
00:57:01 allen morris: Replying to "allen - this ties in..."

They clearly do not know of the concept of T cell hierarchies.
01:00:59 Vanessa Hugo: Sorry I can’t unmute
01:01:22 Robb Owen: Dr. Carter, could you share your email address. I would like to share some front end research we have been compiling to use as antecedent and concurrent treatment with conventional SOC.
01:01:50 Vanessa Hugo: This is a great therapy candidate. Just limited access due to the pre-surgery trial enrollment requirement
01:02:09 Vanessa Hugo: Would love to see this combined with Optune + maybe checkpoint inhibitor
01:03:24 Martin Luzbetak: what is the the dose of IL-2?
01:03:35 Brad Power: wcarter@tvaxbiomedical.com
01:04:18 Robb Owen: Reacted to "wcarter@tvaxbiomed..." with 👍
01:05:14 allen morris: Do you think your process could be optimized by identifying subdominant immunogenic T cell clones and challenging the patient with corresponding epitopes selectively for immune response? This presumes one of the obstacles is "T cell exhaustion".
01:10:57 Ryan Moon (he/him): I know you mentioned glioblastoma, but I was wondering if you’re working with another grade 4 glioma, namely diffuse intrinsic pontine glioma?
01:13:15 allen morris: Do you think delivery of a lower dose to the CSF, a site specific notion of delivery, might be a way to optimize effect, barring the potential toxicity?

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01:13:35 Bill Paseman: What modifications would we need to have to treat kidney cancer?
01:14:34 Dr. Chris Apfel: Wayne, congrats. Keep up with the good work!
01:14:56 Ryan Moon (he/him): Thank you. Very exciting work
01:15:01 Vanessa Hugo: Thank you for the work you’re doing, Wayne.