Tumor Treating Fields and Me: One Patient's Experience

A brief introduction to the Optune device and how it works, its advantages over other available therapies for GBM, and my experience with it

February 10, 2017 By Adam Hayden

Disclaimers, Disclosures, and Caveats: I am not a medical professional or otherwise trained in medicine, treatment, or medical equipment. I am an engaged patient who applies his academic skill set picked up in grad school (philosophy) toward researching the biology and treatment of his brain cancer. My discussion of cancer and tumor treating fields herein reflects my best efforts to digest academic literature and present to a general audience. Corrections and feedback are welcomed. -AH

1. Introduction

Sunday, February 12, 2017, 9pm EST, I will be available during a #BTSM Tweet Chat to field questions during an ask-me-anything (AMA)-style Q&A for patients using the Optune device, the commercial platform for Novucure's Tumor Treating Fields (TTFields) technology for the treatment of newly diagnosed Glioblastoma Multiforme (GBM), a grade IV glioma.[1] In this post I provide a brief introduction to the Optune device and its mechanism of action—that is, how the thing works (section 2), its advantages over other available therapies for GBM (section 3), and the timeline of my experience with the device (section 4). I leave much of my personal experience aside for now to be covered during the chat. My hope is some in the #BTSM audience might find this post ahead of the #BTSM chat Sunday. This post is intended to be helpful for folks who have little information about Optune and TTFields technology.

To proceed with understanding the therapeutic efficacy of TTFields, it is helpful to know what we are up against. Cancer is a collection of many individual maladies that together fall under the taxonomy, cancer. Several illnesses associated with cancer are specific to cancer type, tissue of origin, stage, or grade, but a common feature of all cancers is the unchecked growth ('proliferation') of cells. The reigning paradigm in medical and life sciences research to explain this unchecked proliferation is called somatic mutation theory (SMT) (Note: you may infer from my statement, "The reigning paradigm," suggests other theories are advanced, and this is true. SMT is the dominant theory, and has been growing in evidential support and theoretical sophistication since at least the mid-1950's, but alternative theories deserve discussion; though not in this post. For what it is worth, my recent academic work in the philosophy of science explores alternative theories of carcinogenesis.) SMT asserts that cancer results from the clonal expansion of a

transformed, (‘mutated’) progenitor cell. What does that mean? On the dominant view, a single cell (the progenitor) is genetically damaged (is transformed). The offspring of the progenitor cell (the ‘clones’ in ‘clonal expansion’) carry this genetic damage. The damage occurs to genes that control how a cell grows and divides.[2] Damage to ‘oncogenes’ puts the cell in a state of rapid proliferation. Damage to tumor suppressor genes inhibits the cell from carrying out programmed cell death (‘apoptosis’), the cell’s natural checkpoint to guard against cancer. A helpful analogy appearing in the literature is that of a car: slamming on the accelerator (oncogene damage) while cutting the brake lines (tumor suppressor damage). The result is unchecked cell proliferation, cancer.

2. Optune, Tumor Treating Fields, and Mechanism for Action

Optune was approved in October, 2015 by the FDA for treating newly diagnosed GBM. GBM is the most aggressive form of brain cancer in adults, and it is associated with a very grim prognosis. Few patients live beyond one or two years after diagnosis.

It is also the type of brain cancer I have. Dammit.

As discussed in the previous section, cancer is a disease of cellular growth. Glioblastoma is the highest grade glioma named for the glial cells from which these tumors arise. Glia are 90% of the cells that comprise the brain. These cells support normal brain functioning by insulating, protecting, and facilitating signaling between neurons and other cells types of the central nervous system. Because glia are abundant in the brain, glioblastomas live, travel, and expand effortlessly through the tissue of the brain. This characteristic makes them especially resistant to treatment along with other therapeutic obstacles such as the difficult-to-penetrate blood-brain barrier.

The standard of care (SOC) therapy for GBM is the tried and true slash and burn approach: surgical resection and radiotherapy. My tumor was 71mm just prior to resection. That is roughly the diameter of a baseball. Sheesh! My talented surgeons successfully completed a ‘gross total resection’ of my tumor meaning greater than 90% of the tumor was removed. Unfortunately, GBM has tentacles that branch out from the primary mass. Number one tricky! These tentacles cannot be surgically removed without damage to surrounding healthy brain tissue, so rather than face permanent left-sided paralysis, surgeons and I made the decision to stop the procedure after removing roughly 95% of tumor. I was able to discuss this decision with surgeons during the procedure because I was consciously sedated for surgeons to functionally map my sensory and motor cortex while resecting tumor. The resection was, on balance, a success, despite knowing that residual tumor remained.

Here Optune/TTFields debut just after surgery and a six-week daily chemo + radiation cycle: to help delay if not stop the division of GBM cells that make up these tentacles of residual tumor. Optune is started during the maintenance chemotherapy stage. I have discussed ‘maintenance’ Temodar/temozolomide (TMZ) chemotherapy in previous posts—this is the 5/28 cycle. High-dose TMZ is administered for the first five days of a 28 day cycle: one week on, three weeks off; one week on, three weeks off; a monthly cycle repeating for six to twelve months. During this time Optune demonstrates improvement in two important metrics: overall median patient survival (OS)

and median progression free survival (PFS), meaning the median patient survival time without disease progression.

Here is the important sound byte from a Journal of the American Medical Association (JAMA) article: Median overall survival in the per-protocol population was 20.5 months in the TTFields plus temozolomide group (n = 196) and 15.6 months in the temozolomide alone group." [4]

In plain speak these results demonstrate that among trial participants, those combining maintenance TMZ with Optune/TTFields display a median overall survival of 20.5 months. The population using only TMZ display a median overall survival of 15.6 months. The folks using Optune experienced a 5 month increase in median survival time. These are patient averages from a random sampling of the clinical trial population. Some folks did better, and some folks did worse.

Aside

Through the magic of Facebook I connected with a friend of a friend who was previously a complete stranger, whose husband was in the pivotal EF14 clinical trial which led to Optune's approval. Incredibly what a small world it is that we should be connected through a social media mutual friends. Even more incredible is that this new friend lives in Arizona, where I grew up, and she is familiar with many of the places I am. Pretty cool, huh?

End Aside

This raises the question, how does Optune increase median survival time? How does it work to slow the growth of GBM? The device must be worn at least 18 hours each day to receive benefit. The patient's scalp is shaved, cleaned with alcohol, and four 'transducer arrays'—one set of arrays on the front, another on the back of the head, and one set of arrays on each side of the head, equaling four total arrays. The arrays are held to the shaved scalp with medical grade adhesive and are insulated with an electric-field conducive gel. An alternative field is generating front/back and right/left targeting the area of likely tumor recurrence—for most with GBM this target is a 2cm margin around the resection bed, or surgical cavity. Rapidly proliferating cells is the common feature of cancer, and cells proliferate by dividing in a process called mitosis. For mitosis to occur DNA in the nucleus of the cell is copied into an identical pair, then these things called microtubules line up outside the cell nucleus and start to pull at the nucleus, one strand of microtubules on each side, in a microscopic game of tug-of-war. The nucleus is pulled in two, one copy of DNA on each side, and the cell divides into two identical pairs. To get the microtubules in the proper structure the cell uses the natural electric potential in the tubules. The Optune/TTFields alternating electric fields disrupt the structural formation of the microtubules and the cell is either unable to divide, or divides aberrantly with lop-sided distribution of genetic material and so the cell enters a cycle of programmed death. The result is the delaying or complete inhibition of cancerous cell division.

A natural question is to wonder how the Optune is able to target only cancerous cells. TTFields target mitosis in dividing cells. Resting cells are purportedly unaffected by the frequency and intensity of TTFields. Here is a nice video from Optune, which explains the process more helpfully than maybe I have in this post. (If MDs or PhDs join us Sunday I want to ask how it is that other

dividing cells, even the slow ones like neurons, and other glia that may be facilitating neuronal activity are not affected?)

3. Advantages Over Standard Therapies

The advantage over other therapies amounts to the non-invasive and non-toxic characteristics of Optune over standard of care therapies. Chemo targets rapidly dividing cells in the body, and unfortunately for your typical cancer patient, we possess all sorts of rapidly dividing cells, like hair follicles and the lining of our stomachs. This is why cancer patients often experience hair loss, nausea, and other damage caused by the toxic nature of the therapeutic drugs. I often joke (because high grade brain cancer requires a sense of humor) that if the brain cancer doesn't get me, the bone marrow cancer, a side effect of my chemo, will.

Moreover, in recurrent GBM—'recurrent,'that is, a regrowth of tumor after standard of care has been completed, patients may not be well enough to tolerate additional surgeries or chemotherapy. Also, recurrence may not form a solid tumor mass but may be diffuse throughout the brain, preventing surgical options. Fields generated by Optune may impact cancerous cells in locations unable to be reached surgically or for patients unable to tolerate additional therapies.

4. My Personal Timeline

I have discussed my journey elsewhere in this blog; I will not say much more in this post, but I will render a rough sketch of my treatment timeline. After complaining of seizures and headaches for some time, and especially after failing a typical 'neuro check' with my primary care physician on May 13, 2016, I was ordered to receive a "stat" MRI. That MRI revealed my tumor, and I was in brain surgery less than two weeks later. The pathologist confirmed GBM following surgery. I underwent the standard chemo and radiotherapy and completed the six week daily radiation on August 9, 2016. My neuro-oncologist ordered Optune, and after taking some time to think it through, I agreed and was fitted in October, 2016. I diligently used the device for three months, but my compliance began to waiver around Christmas time. For the first couple of months of 2017 my Optune compliance has been poor. I met with my point of contact, equipment specialist from Novocure this week, and I expressed my sort of "I'm on the fence" attitude to him. Our #BTSM chat actually hits at a pivotal time in my continued use of Optune, and I hope to gain insights from others.

So that's that. A quick intro to Optune, and even if you aren't in the target patient population to use the device, maybe this post has provided you with enough information to "listen in" Sunday evening, 2/12/17, 9pm EST.

Notes

[1] Press Release. October 5, 2015. FDA approves expanded indication for medical device to treat a form of brain cancer.
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm465744.htm

[2] What is Cancer? from National Cancer Institute (NCI), a division of the National Institutes of

Health (NIH). https://www.cancer.gov/about-cancer/understanding/what-is-cancer

[3] The Cancer Genome Atlas Program Overview.
https://cancergenome.nih.gov/abouttcga/overview

[4] Stupp, et al. 2015. “Maintenance Therapy With Tumor-Treating Fields Plus Temozolomide vs Temozolomide Alone for Glioblastoma.” JAMA. https://www.ncbi.nlm.nih.gov/pubmed/26670971

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