Robert Hoover: So, good morning and welcome Committee chairperson, CAC members, guests, both on the phone and watching live via the CMS YouTube channel and here in the auditorium. I'm Dr. Robert Hoover. I'm the medical director of the Jurisdiction C, DME MAC, and I'm the lead administrative medical director for the Jurisdiction C and DME MAC Tumor Treatment Fields, local coverage determination.

Robert Hoover: Thank you to CMS and the coverage and analysis group staff for hosting the meeting today and providing the livestream via the YouTube channel at CMS. The link will also be available on the DME MAC websites after this meeting. My colleague, DME MAC medical directors, and I have convened this Contractor Advisory Committee, or CAC, to discuss the evidence underpinning tumor treatment fields therapy, sometimes called alternating treatments field therapy, for the treatment of newly diagnosed glioblastoma multiforme.

Robert Hoover: Our agenda today includes introduction to the CAC chair and members of the panel, a presentation from Novocure, the manufacturer of Optune®, and the requestor for the LCD reconsideration. Following the presentation, we'll take a short break and then resume with the opportunity for the CAC members to ask questions of the Novocure representatives.

Robert Hoover: You'll note on the agenda today, I have a 10:05 shelter-in-place drill. That drill has been canceled, so we will not be having the shelter-in-place. Following lunch, the CAC chair will lead the panel in a discussion of the key questions, and after the key questions are discussed and rated by each individual on the CAC, I'll wrap up, and we'll talk about next steps.

Robert Hoover: All CAC members have traveled to this meeting without reimbursement by the DME MACs or CMS, either in compensation for their travel or an honoraria for their participation. All CAC members have given consent for recording of this meeting and for the aggregation of scores of each key question to be made public in our proposed LCD.

Robert Hoover: When I introduce the CAC members in a few minutes, I will ask them to disclose any conflicts of interest related to this topic, and if they've been approached by the requestor or any parties other than the DME MACs to discuss this topic after their selection for the CAC panel. Note that while we solicit nominees from the CAC from various clinical organizations, national organizations, and government agencies, the CAC members are here as individuals, and their opinions do not necessarily reflect those of their sponsoring organizations.

Robert Hoover: We ask that the presenters adhere to the time limits. We have a very tight agenda today, and therefore, we don't have a lot of extra time. I'll be timing in the back, so those that are here from Novocure for their presentations, I'll hold up when there's five minutes left and when there's two minutes left. During breaks, we ask that CAC members do not discuss amongst themselves the topic at hand. All discussions will need to take place during the formal CAC sessions.

Robert Hoover: Some final housekeeping reminders for today: First, please make sure that you signed in outside the auditorium so that we have account of those that are participating today. Second, please remember to discard your trash in the trashcans located outside the room. Guests are prohibited from taking photographs on the CMS campus, that includes this auditorium. And lastly, all CMS guests attending today's CAC meeting are only permitted in the following areas of the CMS building: the main lobby, the auditorium, the lower-level lobby, and the cafeteria.

Robert Hoover: Now, I'll introduce our national CAC panel starting with the chair, and Dr. Chakravarti's here, thank you.

Robert Hoover: Dr. Julie Kessel is the Chair for this committee and the Senior Medical Director at Cigna Healthcare. Dr. Kessel is the national medical director in coverage policy, having been involved in policy development since 2010. She oversees the medical, prevention, drug and biologic reimbursement, medical inquiry, and clinical coding teams. Dr. Kessel is a board-certified psychiatrist by training with clinical specialties in research, psychopharmacology, pain management, and forensic psychiatry.

Robert Hoover: Dr. Kevin Camphausen is the Chief of the Radiation Oncology Branch in surgical oncology programs at the National Cancer Institute. As Chief, Dr. Camphausen guides the branch's clinical and translational research program, which studies the role of new agents as both radiation sensitizers and radiation protectors. Dr. Camphausen studies the interaction of novel drugs and radiotherapy in the treatment of glioblastoma multiforme in the laboratory using pre-chemical model systems, and in the clinic, running clinical trials.

Robert Hoover: Dr. Arnab Chakravarti is Professor and Klotz Family Chair in Cancer Research at Ohio State University's Comprehensive Cancer Center. He's Director of the Brain Tumor Program at the (Arthur G.) James Hospital, Richard L. Solove Research Institute. As a member of the James Transitional Therapeutics Program, he focuses on translational cancer research to identify novel biomarkers that are predictive of treatment efficacy and survival, and to uncover molecular and genetic mechanisms of treatment resistance.

Robert Hoover: In his spare time, which I'm sure he has a lot of, he serves on the National Cancer Institute Advisory Board of Scientific Counselors and co-chairs the NRG Oncology Brain Tumor Committee, a non-for-profit research organization formed to conduct oncological clinical research and to broadly disseminate study results for informing clinical decision-making in healthcare policy.

Robert Hoover: Dr. Annick Desjardins holds appointments as Associate Professor of Neurology and Associate Professor of Neurosurgery at the Preston Robert Tisch Brain Tumor Center at Duke Cancer Center, where she is also the Director of Clinical Research. She is a fellow of the Royal College of Physicians of Canada in Adult Neurology, and she's certified in the subspecialty of neuro-oncology by the United Council of Neurologic Subspecialties.

Robert Hoover: Dr. Marc Fishman is founder of Oncology Analytics. After many years in practice as a board-certified internist and hematologist oncologist, Dr. Fishman founded Oncology Analytics with the goal of assisting health plans, and their providers manage the total cost of cancer care by providing access to current evidence-based, disease-specific analytics on all cancer types and treatment options.

Robert Hoover: Dr. Henry Friedman is the James B. Powell Junior Professor of Neuro-Oncology in the chief division of Medical Neuro-Oncology at the Preston Robert Tisch Brain Tumor Center at Duke Cancer. Dr. Friedman is internationally recognized for his contributions to brain cancer research. In addition to his clinical duties at the Duke Cancer Center, where he and his team care for over 900 new-to-Duke patients annually with primary brain and spinal cord tumors. Among other research interests, he studies the role of temozolomide and mechanisms of resistance in glioblastoma, and the role of bevacizumab in the treatment of glioblastoma.

Robert Hoover: Dr. Cary Gross is Professor of Medicine and Epidemiology and the Director of the National Clinical Scholars Program at Yale. He's also the Director of the Yale Cancer Outcomes Public Policy and Effectiveness Research Center. The overarching theme of Dr. Gross's work is the disconnect between evidence generated from clinical research and the actual needs of older persons with cancer. He uses comparative effectiveness studies and policy-relevant research to address this important knowledge gap. He also has a longstanding interest in research ethics and integrity, and is a collaborator on the Yale Open Data Access, or YODA project, which aims to promote and advance the sharing of clinical data.

Robert Hoover: Dr. Matthias Holdhoff holds an appointment as an Associate Professor of Oncology and Associate Professor of Neurosurgery at the Johns Hopkins University School of Medicine. Dr. Holdhoff practices as a medical oncologist in the brain cancer program at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins in Baltimore. Dr. Holdhoff's expertise is in primary brain cancers and central nervous system lymphomas. He completed his primary medical training in Germany before coming to the US for residency and medical oncology fellowship at Johns Hopkins. He's board-certified in internal medicine and medical oncology.

Robert Hoover: Dr. Edjah Nduom is a staff clinician at the Surgical Neurology Branch Tissue Bank at the National Institutes of Health, National Institute of Neurological Disorders and Stroke. Dr. Nduom's research interest is conducting translational studies to develop novel approaches for the treatment of primary brain tumors. Early in his career, he focused on the blood-brain barrier and drug delivery, a topic of interest for many clinicians attuned to the difficulties in treating malignant brain tumors. More recently, his work involved clinical trials of cerebral micro dialysis in glioblastoma patients to test the blood-brain opening ability of regadenoson.

Robert Hoover: Mr. Parashar Patel, our industry representative, is President and CEO of Market Access Strategies, LLC. Market Access Strategies provides healthcare, market access, coding coverage, and payment strategies to medical device, biotechnology, and pharmaceutical companies. Mr. Patel started his career in government service, first at the state level, and later at the federal level, working for the Office of Management and Budget, the staff of Senator George Mitchell, and at the Healthcare Financing Administration now called CMS.

Robert Hoover: He left CMS in 2003 to join Boston Scientific as their Vice President of Global Health Economics and Reimbursement, culminating his career there as Vice President of Global Health Policy. In that role, he held global health policy and data analytics teams to shape Boston Scientific's commercial strategies in the context of policy trends.

Robert Hoover: Dr. Carlos Peña is Director of the Division of Neurological and Physical Medicine Devices at the Centers for Devices and Radiological Health at the Food and Drug Administration. Dr. Peña and his division support the CDRH vision for patients in the US to have access to high-quality, safe, and effective medical devices of public health importance in this world. Under his leadership, he advances the CDRH's goal of increasing regulatory transparency, including expedited access for pre-market approval of medical devices, intended for unmet medical needs for life-threatening or irreversibly debilitating diseases or conditions.

Robert Hoover: Dr. Jonathan Sherman is Associate Professor of Neurosurgery and Director of the Surgical Neuro-Oncology Unit at the George Washington University School of Medicine and Health Sciences in Washington, D.C. As the Director of the Neurosurgical Oncology Group at George Washington University, he's worked on several interdepartmental collaborative projects to study the effects of cold atmospheric plasma in the treatment of glioblastoma. Through his research in a collaborative approach, Dr. Sherman looks to further define the role of cold atmospheric plasma and the treatment of Glioblastoma and other malignancies.

Robert Hoover: Dr. Paul Zeltzer, our beneficiary advocate, is a neuro oncologist, educator, brain cancer researcher, author, and entrepreneur, whose medical career spans 30 years with expertise in the areas of neuro-oncology, immunotherapy, and clinical trials against cancer. Dr. Zeltzer has authored over 130 publications on the molecular biology treatment results in long-term outcomes of cancer, including editing two major textbooks in oncology and neuro-oncology. He's been the principle investigator in several NIH funded studies in leukemia and brain tumors. He and his wife, Dr. Lonnie Zeltzer, founded the non-for-profit Whole Child LA Foundation to provide support and payment for complimentary therapies for children with chronic pain. Dr. Zeltzer also has an entrepreneurial side, having been involved in several startups and commercial ventures in the area of web and mobile application-based cancer informatic tools.

Robert Hoover: I'd now ask that each CAC member disclose, for the public record, any significant conflicts of interests with the topic today, and any contacts you may have had with any representatives, Novocure or otherwise, since your selection for the CAC panel, and we'll go in seating order, starting with Dr. Chakravarti.

Dr. Arnab Chakravarti: No conflicts.

Dr. Edjah Nduom: Uh, no significant conflicts. I did receive communication from the National Brain Tumor Society on their position on this panel.

Dr. Matthias Holdhoff: No conflicts with Novocure. I am on the advisory – I was on the advisory board meeting with [inaudible] Cellgene and BTG. I did receive an invitation to meet with the CEO of Novocure in February, and it was after I was invited to participate in this meeting, and we did not meet.

Dr. Cary Gross: I have conducted research that's funded by Pfizer and Johnson & Johnson. I have received travel funding from a company called Flat Iron. I have received emails from the President of the National Brain Tumor Association in the past couple of days, and my personal conflict is that, six weeks after my wife and I were married, her sister was diagnosed with glioblastoma, so I have a personnel overlap with this topic.

Dr. Camphausen: I have no financial disclosures. I'd received the same email from the Brain Tumor Society yesterday, and I spoke with Dr. Ballo this morning, saying hello.

Dr. Cary Gross: I also received the email from the Brain Tumor Society.

Robert Hoover: Yeah, I think all of the four DME MAC medical directors and the CAC members received the same letter advocating on behalf of their members. Thank you.

Dr. Julie Kessel: I have no conflicts.

Dr. Annick Desjardins: I have no conflicts with Novocure. I have not been contacted by Novocure since the CAC members, were identified. I do have a research support from different agents, uh different pharmaceutical companies, PTC Therapeutics, Celgene, Pfizer, Celldex, Genentech, but otherwise, no other conflict. And I have stock options in [inaudible] oncology.

Dr. Paul Zeltzer: Yeah, Paul Zeltzer, no conflicts, no emails.

Dr. Henry Friedman: Henry Friedman. I received the email. I have a number of conflicts that are not relevant to this meeting with other companies. I was approached, nothing with Novocure. I was approached by one of the Novocure people to talk with the CEO. But before, to my knowledge, the CAC membership was listed, and that meeting never occurred.

Dr. Jonathan Sherman: Jonathan Sherman. I did receive the email, no conflicts.

Parashar Patel: Parashar Patel, no conflicts and no emails.

Dr. Marc Fishman: Marc Fishman, no emails, no conflicts.

Dr. Carlos Peña: Carlos Peña, no conflicts. I did get a copy of the email too.

Robert Hoover: Thank you very much. Now I'll turn it over to my colleague Dr. Mamuya for an overview of why we're here today.

Fred Mamuya: Good morning, everybody. My name is Fred Mamuya. I am one of the medical directors for Durable Medical Equipment, Jurisdiction A. I would like to start out by apologizing if I offend anyone. Please don't attribute that to my fellow medical directors, and for sure don't attribute that to CMS.

Fred Mamuya: I would like to begin by thanking our CAC members. Some of you walked through snow to get here. Some of you flew from L.A. to get here on red-eyes, uncompensated but willing to help us in this endeavor. I also wanted to point out that your views are expressly yours; they won't be attributed to your organization or any other affiliations you might have, so please feel free in your deliberations. So, with that said, I would like to point out to two or three definitions before we get going, because that came up during the pre-meeting.

Fred Mamuya: The first one is TTFT. We will just call it TTFT, but we're really talking about tumor treatment field therapy. The second is LCDs. LCD is an acronym for local coverage determinations. Those are the policies that we, the DME MAC contractors write to cover our different jurisdictions. In the DME world, they are identical, so we only refer to one LCD. Someone asked me, why do you call it an LCD? And that's the reason why. And the last is CAC. That's a contract advisory committee. It's a new process that's new to the DME MACs. I think, in 2016, the Cures Act was passed, and along with the Cures Act was a change in how LCDs are developed or reconsidered, and that gave us an opportunity to avail ourselves to a CAC process, and that's what we are doing here today.

Fred Mamuya: So, why are we here? The CAC is really here to help us evaluate the quality of evidence as it currently stands, when it comes to TTFT for the treatment of newly diagnosed Medicare beneficiaries with glioblastoma. The CAC is not here to approve a policy, so this exercise will really be a discussion about the quality of the evidence.

Fred Mamuya: The background is in August of 2014, the DME MAC medical directors came out with a policy for TTFT, which indicated that, for Medicare beneficiaries, TTFT was not reasonable and necessary. Those are the familiar words we use in Medicare speak. Last year, Novocure approached the medical directors to request that we reconsider the policy, to revise it to include the fact that TTFT is reasonable and necessary for the treatment of newly diagnosed Medicare beneficiaries with glioblastoma. Along with the request, Novocure sent four supporting publications. Three of them were based on a single clinical trial.

Fred Mamuya: There was a 2015 interim reporting of the trial. That was one publication. There was the final report in 2017. That was the second publication. And there was a subsequent secondary analysis in 2018, and that was the third publication from that one clinical trial. Along with Novocure submission was also a copy of the National Cancer Comprehensive Network Guidelines from 2018. The medical directors conducted their own search, and we came up with a list of another 25 publications or so. They're posted on our website. And so, the 29 pieces of clinical literature really formed the basis of what we will be discussing here today.

Fred Mamuya: So, it is our hope that the presentation from Novocure, the extensive and robust discussions by our CAC members, will lead to a scoring of the Key Questions, and the questions are phrased like, “How confident are you that x, y, z”, and the scores are one to five. One is low confidence and five is very high confidence. And those results will be tallied, averaged and we will be sure to include them in any proposed LCD that we post, and I think a Dr. Hoover, in the afternoon closing remarks, will address how that process will unfold after the CAC.

Fred Mamuya: I think, before I hand it over to Novocure, a few final housekeeping points. One, please mute your phones. If you need to take a phone call, please step out in the hallway. So, that's the first. The second is, as Dr. Hoover pointed out, we're not allowed to wander in CMS, so the public bathrooms are on your way out to the left; before you make the left, to head up to the lobby. And the last is once again, please remember to register outside if you did not do so on your way in. I'm going to invite Novocure to come up with their presentation. I will ask every speaker to identify themselves with a title, introduce themselves, and then proceed. Thank you.

Bill Doyle: Good morning. My name is Bill Doyle. I'm the Executive Chairman of Novocure. I'm going to start this morning by introducing the Novocure speakers. Myself, as I mentioned, Bill Doyle, Executive Chairman of Novocure. Earlier in my career, I was Executive Vice President of Johnson & Johnson with responsibility for R&D and licensing and acquisitions of their medical device group. Literally, my labs have, and during my 25-year career, I've been involved with over a thousand medical technology products that have been approved by the FDA and brought to market.

Bill Doyle: I'm joined by Dr. Matt Ballo, Professor of Radiation Oncology at the University of Tennessee Health Science Center, and also the Medical Director of Radiation Oncology at West Cancer Center.

Bill Doyle: We're also joined today by a Novocure patient. It's one thing for those of us who do not suffer from GBM to discuss the patient experience theoretically, but Steve has joined us today to give the perspective of an actual patient.

Bill Doyle: And finally, Dr. Adrian Kinzel, also from Novocure, trained as a neurosurgeon, and has a significant responsibility in our R&D organization.

Bill Doyle: Just to, um, let me go back here. I'm also going to start with just a little bit of level setting. Again, things I think most of us know, but just to make sure there's no confusion. Again, tumor treating fields is referred to in the literature, in the materials by a number of acronyms. We, again, call it tumor treating fields. You'll see sometimes TT fields, TTF, TT fields treatment, and CMS and the I MACs have invented a new acronym, which is this TTFT. It's all the same thing. Optune®, which you'll also hear, is the name of the delivery system. So, that's the product name that delivers tumor treating fields. And we'll talk today a significantly about EF-14. This is the electric field 14. This is the randomized clinical trial that was performed in newly diagnosed GBM, and it will make up much of the clinical discussion today. And then, of course, everyone knows glioblastoma, GBM, and also referred to in the old name, glioblastoma multiforme, all the same disease that we're discussing today.

Bill Doyle: I also want to clarify here that the LCD request, our request for Medicare coverage is for TTFT with temozolomide, is covered for the treatment of adult patients with newly diagnosed supratentorial glioblastoma, following maximal debulking surgery and completion of radiation therapy, together with concomitant standard-of-care chemotherapy. I want to point out that this is exactly the same request as is covered in our FDA label. Many times, again, the CAC process is new for DME. Med CACs have been part of the process for many years for drugs, and very often, they're convened when there is an extension of a therapy or a new application prior to FDA approval. Today's request is perfectly consistent with the product's FDA approval.

Bill Doyle: Secondly, I want to give a little bit of background on the PMA process. Obviously, we have a representative of CDRH, but in the treatment of tumors have been historically focused on drug development. And so, for those of you who are less familiar with the standards, the FDA standards for medical devices, sometimes people think that that's an easier pathway, and there is a pathway called the 510(k), when a new device is really an evolution of an old device. The PMA pathway is essentially equivalent to the NDA pathway on the drug side. This is the most stringent pathway for medical technology, and it's for class three devices that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential unreasonable risk of illness or injury.

Bill Doyle: PMA approval is based on a determination by the FDA that the PMA contains sufficient, valid scientific evidence to assure that the device is safe and effective for its intended use. So, the Optune® approval for the treatment of newly diagnosed GBM went through the PMA pathway, a pathway that involved a panel of FDA experts, months and months of evaluation of the data down to the CRF level, full inspections of the clinical sites. So again, just a little bit of background.

Bill Doyle: And finally, I want to echo, too, the reason that we're convened here today. We're here to present to you in support of our LCD reconsideration request. The general acceptance standard for LCDs, according to the Medicare manual, is as follows: “In conducting a review, MACs shall use the available evidence of general acceptance by the medical community, such as published original research in peer-reviewed medical journals, systemic reviews, and meta analyses, evidence-based consensus statements, and clinical guidelines.” So, that's what we're going to underline this morning.

Bill Doyle: So, I'm going to start with the questions that we were provided on Friday. I will say here that I've been involved in this project now for 18 years. As I mentioned, the FDA spent months in evaluating the evidence. JAMA also spent months, brought in consultants to evaluate the data. We could provide a PhD seminar over weeks on TT fields, and we're going to try in an hour this morning to give you an overview. But it's a tough ask.

Bill Doyle: So, let me start with question number one. “How confident are you that scientific evidence supports mitotic spindle disruption and cellular apoptosis as the mechanism of action for TTFT?” Our answer is that we are extremely confident. I'll start with the following, which is the concept, or the notion, that forces disrupt spindle tubule formation is not new. There is an extensive scientific literature. If you go to Medline, we did this on Friday, you come up with 473 publications, including publications in science, nature, nature reviews, all that demonstrate that forces applied to tubulin disrupt microtubule spindles. And in fact, I just pulled one graph from a science presentation, where the specific force has been calculated and published. It turns out it's 3.4 piconewtons applied to a tubulin dimer will disrupt a spindle formation. So, that concept is completely elucidated in the peer-reviewed literature.

Bill Doyle: The second thing that I'll remind everyone, and this will take us all back to our freshmen physics, is that forces that we just discussed can be applied at a distance by fields. Of course, we're all familiar with gravity, the force that is applied between masses. We're also all familiar with magnetic fields, the force that's applied between a magnet and a ferromagnetic object. So, if I have a nail and a magnet, the magnetic field will apply the force that pulls the nail to the magnet. Electric fields are analogous to these more familiar fields. In the case of an electric field, if I have a plate here with a negative charge and a particle with a positive charge, the electric field force, will pull on the negative charge and pull it to the positive charge. Important for biology, if we have a dipole, and of course, many of our proteins are dipoles, they have a charge, a positive charge on one end and a negative charge on the other. In an electric fields, dipoles align in the electric fields, and this was the fundamental insight that allowed for the invention of tumor treating fields therapy.

Bill Doyle: In tumor treating fields, we create a circumstance through a medical device that allows an electric field to penetrate through a cell membrane and apply forces on the charged proteins within the cell. Now, it turns out, cells, depending on their function, have different electrical properties, and therefore we're able to tune the electric fields to get into specific cells, so this gives us our ability to differentiate between cancer cells and normal cells. But when the field does penetrate the cell, and the cell, balls-up for cell division, of course the nuclear membrane disintegrates, the chromosomes line up in the middle of the cell, and in normal division, the spindle forms from the tubulin subunits, attaches to the chromosomes, and separates into the daughter cells. When tumor treating fields are present, those tubulin dimers cannot form a functional spindle, and we see a strong apoptotic destruction of the cell.

Bill Doyle: This is easily observed. It's never quite as good on one of these big screens than it is on a computer screen, but on the left, you can see a figure that you're all familiar with, the genetic material in the middle, the tubulin is stained green, that's attached to the chromosomes. In a cell exposed to tumor treating fields, you can see the complete disruption of the tubulin spindle, and in this particular cell, the desegregation of the chromosomes, so clearly from your side, the pulling of the majority of the genetic material one direction, the lack of genetic material in the other direction, this cell will die as a result of this aborted chromosome segregation.

Bill Doyle: This mechanism is a fundamental mechanism. Obviously, all cells require a functioning spindle in order to divide. We've observed this in every single cancer cell line that's been tested, and we have observed the effect in every animal model tested as well as in every human first-in-man phase-two trial, and of course, the phase-three trials that were performed.

Bill Doyle: Now, while these figures you might recognize, because they look very similar to the figures that you see with taxanes, which are also spindle poisons. In our case, we deliver our therapy via a medical device. The device has two components. On the right, you can see there's a small box, the current generation weighs about 2.7 pounds, that generates the specifically tuned electric field, and then it is connected to what are essentially bandages with very specific transducers that are affixed externally to the skin surrounding the region of the tumor. We deliver the fields in two directions, so the fields will alternate, in the case of brain cancer, from side to side and front to back, and this is how patients receive the therapy, continuously over time. The other thing I'll mention here too is one of the benefits, and again, I'll compare it back to taxanes, which are actually very effective antimitotics, but they come with a significant systemic toxicity.

Bill Doyle: In the case of the Optune® system, we see no systemic toxicity. Dr. Ballo will show you the AE reports from the clinical trial. The one toxicity that we do see, or side effect that we do see, is local contact dermatitis in approximately half the patients under the transducer arrays. And again, if a patient has a band-aid on their head for two years, that is something that we expect. It's always mild to moderate or substantially mild to moderate, and is treated with the typically over-the-counter skin therapies. And again, Dr. Ballo can speak to this.

Bill Doyle: Now, one question I receive, and often we have our brain often, we're thinking about radiation therapy, the other dominant physical modality. In the case of radiation therapy, there's always a penetration issue. Electric fields are different. If we have a plate, and a second plate that's separated by 10 centimeters, and we have a 10-volt difference, there'll be one volt per centimeter of electric field, throughout that distance. There's been a substantial number of questions about can you really get the field through the skull into the brain. When we started this work 15 years ago, we actually did measurements on patients during brain surgery. So, we would place, to test this, an electric field measurement probe inside the brain. Since then, there's been quite a bit of independent publications that now allow modeling. This is done by NIH researchers, but shows the distribution of electric fields within the brain, based on the location and the intensity of the electric fields that are applied. So, the message here is that we can clearly get a therapeutic dose of electric fields into the brain.

Bill Doyle: So, one of the questions that was posed was that we originally applied in 2014, for our, LCD application. The reason we're back is that from 2014 to 2018, there's been significant additional research and data available for CMS's consideration. Most of it is independent. So, we now have over 30 academic centers that are performing basic research on tumor treating fields. In your materials, I've listed a few, but from Korea University, a comprehensive revalidation of the mechanism of action, again, independent. Stanford's working on the effects of TT fields on other agents, so the combination therapies. The University of Wurzburg, they're specifically working on TT fields with checkpoint inhibitors. UT Southwestern has focused on the effects in synergy of tumor treating fields and radiation. And then we have work in Germany at Max Planck on maximizing the field density within the brain, particularly in the tumor bed.

Bill Doyle: Finally, again, and we'll go back, when this was first considered in 2014, virtually all of the research on tumor treating fields was generated by Novocure. We invented the therapy. We did all the initial research. One of the big things that has changed since 2014 is now the majority of peer-reviewed publications are from external authors. We didn't have the opportunity to provide the full bibliography to you in advance of this meeting, but in the materials, we provided, you can see the full bibliography. And again, as I said, the majority comes from external sources.

Bill Doyle: So, that's at least some information underlining the first question. Now, I'm going to proceed to the second question. "How confident are you that TTFT is generally accepted by the medical community for newly diagnosed GBM?" And again, I'm going to report on the difference between 2014 and today in 2018. And we believe, in 2018, again, the answer to this is a resounding yes.

Bill Doyle: I'm going to provide you with the development timeline here. In some cases, because we are working in an area of electric field therapy that is not quite as much in the mainstream or historically in the mainstream,some people have called this, some sort of an overnight success or an overnight therapy that's come on the scene. I want you to rest assure that, where we are today, which is with a category one NCCN guideline recommendation based on now five-year follow-up data to our EF-14 randomized phase-three trial published in JAMA, has been the result of 18 years of dedicated research from the Novocure team and external authors.

Bill Doyle: Again, here we can see that, in 2014, only a small percentage of the total number of GBM patients received a prescription for GBM. Today, there has been tremendous advance within the field. And in 2018, fully 40% of the eligible patients diagnosed with newly diagnosed glioblastoma in the U.S. received a prescription for GBM. Earlier, I mentioned my experience in the med tech industry. This is the fastest adoption of a medical technology that I'm aware of in my career. And this includes pacemakers, ICDs, insulin pumps for diabetics, artificial hips and knees for osteoarthritis. There has not been a faster uptake of a medical technology.

Bill Doyle: The second indication, as you can see, in 2014, when we were first here, there were 172 prescribers in the U.S., a relatively small number. In 2018, there were over 1100 unique prescribers representing a number of specialties, 50% of whom were neuro oncologists, 31% were radiation oncologists, and the balance, medical oncologists in the community and neurosurgeons. So, we've seen just a tremendous uptick in the members of the community that are prescribing tumor treating fields.

Bill Doyle: Secondly, we've seen full geographic penetration of the technology. So, this is not centered in a particular cluster, whether it's in the northeast or the southwest. We received last year prescriptions from every state including Washington, D.C., and Puerto Rico, and that 40% acceptance is balanced among the east, the central, and the west regions. So, this is now a therapeutic option for patients that has become part of the therapeutic landscape across the entire country.

Bill Doyle: We also see that newly diagnosed GBM, which is treated both in academic centers and in the community, that Optune® therapy for newly diagnosed GBM has now become part of the standard practice, both in the academic centers and in the community. We see it's roughly 50-50, 50% from the academic community, 52%, 48% from the community. And importantly, this is a therapy that the FDA has mandated that prescribers must be certified or trained prior to prescribing. And we have trained certified prescribers now in 59 of the 62 NCI designated cancer centers. So, with a few, with the exception of a few laggards, full training in all the NCI centers.

Bill Doyle: The final point I'd make is that this penetration over a very short period of time is even more extraordinary by virtue of the fact that prescribers received zero revenue from prescribing this product. So, the reasons that this is becoming part of the clinical practice is a direct result of the benefits seen for patients in both the clinical research and in practitioners' own experience. Again, this is very typical of med tech products, but also typical of many drugs that, as you know, clinicians will of course read the data. They'll read the label, they'll be very cognizant of the FDA approval, but then they'll try it and they'll use it and they'll see the effects on their own patients. And then, adopt it. And in this case, with no, and this contrasts directly with infused chemotherapies, which is an area where physician practices receive a fraction of the revenue that is derived from prescription.

Bill Doyle: So, the final point I'm going to make here, and then I'll turn it over to Matt for the heavy lifting on the clinical data, is that this therapy is now paid for and reimbursed by essentially every single private payer in the United States. Both of the parent corporations of the organizations who organize the CAC here, cover Optune® for newly diagnosed GBM. Every single one of the big five, and we know how hard that can be, cover Optune® for the treatment of newly diagnosed GBM. A further 85 small plans, all the blues, cover Optune®, and it equates, and in fact, I just had an updated number since we put this together. It's now approximately 250 million Americans are covered for Optune®. The only significant payer today that does not cover Optune® for the treatment of newly diagnosed GBM is CMS. And that's why we're here. We think there's a significant risk of putting Medicare beneficiaries at risk for inequitable access if we collectively don't act.

Bill Doyle: I will note that I made the personal decision as we were developing the evidence, and as we were training the community, to provide Optune® to the Medicare-eligible population at our risk. But this is something that is a small company that's never made a profit that we can't continue to do indefinitely.

Bill Doyle: So, as I said, I'm going to move now to the next question. And here, “How confident are you that there is sufficient evidence to determine that TTFT for newly diagnosed GBM can provide net positive health outcomes in the Medicare-eligible population?” Before I turn it over to Matt, I do want to just underline the definition of what is Medicare-eligible. So, clearly, it's the over-65 population. It's also the end-stage renal disease, which is not of issue here, but it also includes those patients that are permanently disabled, regardless of age. And for those who are familiar with the treating patients with GBM, very often, GBM leads to debilitating side effects, rendering patients unable to function independently, and therefore GBM patients of any age are often Medicare eligibility. With that definition, I'm going to turn it over to Dr. Ballo to review the clinical evidence for TTFT in newly diagnosed GBM.

Dr. Matthew Ballo: Okay. Thank you very much. I am Matthew Ballo, radiation oncologist, Professor of Radiation Oncology at the University of Tennessee Health Science Center, and the Medical Director of the West Cancer Center, which is located in Memphis, Tennessee. So, I am going to talk to you about EF-14, the results of that clinical trial, and try to place that trial into the context of what you all, what we all know already, about GBM and the state of the science. This is obvious, you know that glioblastoma is the most prevalent and aggressive central nervous system cancer in adults. I won't go through the rest of this, but you know the disease prognosis depends on several characteristics that have to be controlled for if you're going to do a randomized trial.

Dr. Matthew Ballo: And just to place Optune® therapy into the context of how the FDA of views glioblastoma, I kind of divide the FDA approval process into three eras. There's the carmustine era, there's the temozolomide bevacizumab era in the middle, and then of course you have now what I think is a very important era, the Optune® and the temozolomide era together. Again, placing this trial in the context of what we know. If you look, this is an article that came out in neuro-oncology last year. If you look at the studies that have been done between January of 2005 and December of 2016, there have actually been eight completed phase-three randomized trials. That's the gold standard of how we judge something that we're looking at in medicine. Of these eight trials, only one was positive and that one positive trial is what we're here to talk about today.

Dr. Matthew Ballo: These are the papers that you have copies of to review prior to today's discussion. 2015 is when the preliminary results were first presented, and that's really when I became most interested in tumor treating fields. Obviously, I'm a clinician, it was the randomized trial that excited me about this result, excited me about this technology, but it was at that time that I started to look at the basic science and to learn about this physical property. Remember, I'm a radiation oncologist, and the fact that there was another physical force out there that could influence dividing cells was absolutely fascinating to me, and that was why I started looking into the basic science. 2017 is when the mature results were presented, and then of course, we've got the quality of life data as well.

Dr. Matthew Ballo: So, EF-14 was not a small trial. This was a trial of 695 patients who had all undergone a maximal surgical debulking. They had all completed their chemotherapy and the radiation therapy. And then after an enrollment window, they were randomized to either Optune®, 18 hours a day, with temozolomide or to the standard of care at the time, temozolomide alone. And at the time of first progression, the patients would continue Optune®, so that's important. They would continue their Optune® therapy, and they would receive salvage therapy, second line chemotherapy, stereotactic radio surgery, but they would remain on the Optune® therapy until their second progression, or 24 months, and that's when they would come off the trial. And the primary endpoint of this trial was progression-free survival, and there was a pre-specified p-value that had to be met before they would look at overall survival. So, the reason there was a preliminary result is because the pre-specified p-value was met, progression-free survival was improved, they then looked at overall survival and overall survival was also improved.

Dr. Matthew Ballo: Again, as I said earlier, patients were stratified by all of the things that we would want them stratified by at that time. The resection status, did they have a biopsy, subtotal resection, gross total resection, and they were stratified by MGMT status, and the MRI review of actually looking at progression-free survival, the MRI review was blinded, so it was centrally reviewed, and they were blinded to whether or not the patient was on the device or not on the device.

Dr. Matthew Ballo: Key baseline characteristics were well-balanced between the two arms, just what you would want to see. You would want to see that the age was well-balanced between the two arms, performance status was well-balanced between the two arms, extent of surgical resection,median time from diagnosis was the same, MGMT status. IDH status was not available in every patient, but IDH1 status was at least balanced between the two arms, and then the use of antiepileptics, again, was balanced between the two arms.

Dr. Matthew Ballo: And it's hard to argue with the results. There's no crossing of the curves, there's no meeting at the end, there was a clear improvement in progression-free survival. The number that we as clinicians are most interested in is the median progression-free survival from diagnosis, 11.2 months versus the 7.8 months. A clear improvement. And again, with overall survival, it's hard to argue there's no crossing of the curves, there's no meeting at the end. There was a clear improvement in overall survival. Median overall survival from diagnosis was 24.5 months, versus 19.8 months for the temozolomide alone. Again, one of the reasons why I was so excited about these results, because as a resident, I was always telling patients that the median survival was 12 months, so now we have a median survival of 24 months. Two-year overall survival clearly improved.

Dr. Matthew Ballo: And what about the side effects? Side effects were just what you would expect. All of the patients who are on temozolomide, so the thrombocytopenia was equal between the two groups, and then central nervous system disorders, such as seizures, were identical between the two groups. My gut instinct was that you're putting this device on the brain that has been operated on, an irritated brain perhaps, and you're going to cause seizures these patients, but the reality is, you don't see seizures, and it actually makes sense that you don't see them, because remember tumor treating fields are too energetic to cause membrane depolarization, and they're not energetic enough to cause any heat.

Dr. Matthew Ballo: Okay, again, let's place this trial in the context of the environment that we have for GBM. If you look at the original Stupp trial from 2005, the hazard ratio, so radiation therapy alone versus temozolomide, the hazard ratio was 0.63, there was a clear improvement in median survival, a clear improvement in two-year survival and five-year survival, and if you compare the magnitude of that benefit to the benefit that we see in the current trial, where we're adding Optune® to the temozolomide, the magnitude of that benefit is identical. We were very excited about temozolomide in 2005, and it quickly became the standard of care, and was accepted almost uniformly across the board, immediately.

Dr. Matthew Ballo: Okay. Also, to place this in context of where we are, if you look at RTOG 0525, that was the trial of dose-dense temozolomide, and James Cox was the Chairman at MD Anderson when I was there, and he would always sit us down and teach us, how do you attack a randomized trial? Critically, of course, he didn't use the word attack. He said, how do you critically assess a randomized trial? He would say you go after the control arm. You say that the reason that there's a p value that's significant is because of the control arm did poorer than they should have. The reality is, if you control, I'm sorry, if you compare the control arm from RTOG 0525, it's actually identical to the control arm of EF-14, suggesting that you can't really go after the control arm. There really is something going on in the patients who received Optune®, so much so that the National Comprehensive Cancer Network has now given it Category 1 status.

Dr. Matthew Ballo: So, regardless of age, if you're over the age of 70 or less than the age of 70, if you are methylated or unmethylated, standard brain radiotherapy with concurrent temozolomide and then adjuvant temozolomide with tumor treating fields, is the standard, or one standard that you can offer these patients. This is in the group over the age of 70.

Dr. Matthew Ballo: Okay. So, "What about predictors of success? How confident are you that the available evidence demonstrates adequate predictors of success in Medicare-eligible population?' So again, I'm kind of describing for you my evolution and my interest in this technology. My gut told me that this is a device, these patients are going to have to wear this device, and that maybe the elderly patient, maybe the patient in the wheelchair, maybe the patient that's only had a biopsy, is not going to really benefit from this therapy. But in fact, I was wrong. If you look at the forest plot from the randomized trial, and this is the subgroup analysis of who benefits and who doesn't benefit from the use of the device, unmethylated or methylated MGMT status, resection status, age, KPS, everyone benefited from the device. And why we're here today is to talk about a Medicare-eligible population, specifically in the patients over 65 years of age. You can see in the forest plot that there was an improvement in the overall survival through the use of tumor treating fields.

Dr. Matthew Ballo: Now, this is where we have to get down into the weeds just a little bit, but I wanted to share with you, I know you're all very familiar with EF-14, but you may not be familiar with some of the new science that has really developed in the last, really, let's say 12 months, 24 months.

Dr. Matthew Ballo: What affects , what modulates the effect of tumor treating fields? Well, one thing is the frequency. So, in this experiment, this is multiple cancer cell lines that are exposed to tumor treating fields at frequencies that vary from 50 to 500 kilohertz. And you can see that it's cell-dependent. If you have a mouse melanoma, mouse melanoma cells are most sensitive to 100 kilohertz. If you have human breast carcinoma, 150 kilohertz. And for why we're here today talking about glioma, 200 kilohertz seems to be the frequency of interest, and so that is the frequency that was tested in the randomized trial. And again, what excited me about the data is this sort of bench-to-bedside translation of what we're looking at. Here, we have, in the laboratory, 200 kilohertz seemed to be the most effective frequency. Now, we have a randomized trial that showed that 200 kilohertz actually did make a difference.

Dr. Matthew Ballo: The second thing you see is a time-dependent. So, the longer cells are exposed to tumor treating fields, the more inhibition of cell division you get. So, these are actually for glioma cell lines, and in all four cell lines, you can see that if you're exposed to the tumor treating fields for 24 hours, 48 hours, 72 hours, 96, 120, that you see a clear inhibition of cell division the longer you wear this, or I'm sorry, the longer that you apply this to your cell culture. The reason I say wear this is because this also turned out to be true in the randomized trial. The longer patients wore the device, the longer they lived. So, the patients that wore it 60% of the time didn't live as long as the patients who wore it 70% of the time, who didn't live as long as the patients who wore 80% of the time, and so on. There was a stepwise improvement in overall survival the longer you wore the device.

Dr. Matthew Ballo: We also see that the increased intensity seems to be dependent. There is something that happens right at around one volt per centimeter, that there seems to be a threshold event at one volt per centimeter, where you have these cell lines that were all exposed to the frequency that they're sensitive to, so the glioma cell line was exposed to the 200 kilohertz, and then you varied the intensity, and as you vary the intensity, you saw that there was an increase inhibition of cell division, and one volt per centimeter was the threshold.

Dr. Matthew Ballo: The last thing that's known is, and all of the patients on EF-14 actually wore a customized array layout. They didn't just place the arrays on right and left lateral, front and back. They actually were given a customized layout of exactly how to wear the array so that you would increase the dose or the intensity to your tumor bed, because it was known that if you just have a symmetric array, you're going to get a certain amount of tumor treating field to the tumor bed. But if you customize that array by moving the arrays forward or moving the arrays back, you can actually increase the field intensity through that region of interest.

Dr. Matthew Ballo: So, we've kind of done the bench-to-bedside discussion of field frequency. The trial's positive. There is evidence, and it's good evidence, that the longer you wear it, the more it works. But as a radiation oncologist, I would want to know that if you actually increased the dose of tumor treating field to the tumor bed, I would want to see that those patients are actually living longer, and that the customized array out does make a difference.

Dr. Matthew Ballo: And so, this was an abstract, and the manuscript is now at the Red Journal, unpublished, but in review, where we correlated tumor treating field dose-density and survival. So, what we did was, the hypothesis basically being that overall survival and progression-free survival are higher in patients who receive a higher dose to the tumor treating to the tumor bed. And so, what we did is we, it's complicated modeling, but what you basically do is you segment the tissues on the patient's MRI scan. So we would segment the contrast-enhancing tumor, segment the tumor bed, and then on a phantom, we would have the segmented scalp, skull, gray matter, white matter, CSF, and then using a deformable registration process, those are merged to create a model that is specific to that patient, and then they are the actual patient-specific array placement is placed onto that model.

Dr. Matthew Ballo: And then using a finite element method, what you do is you take those segmented contours, you turn them into a mesh, and you solve Maxwell's equation across those interfaces between tissues that have a different conductivity, and you are able to calculate the field intensity through that patient's brain and through that patient's tumor bed specifically. And we looked at the tumor bed by creating an expansion around the tumor bed of three millimeters. And we looked at the actual dose of the tumor treating field through that patient's tumor. We looked at both field intensity, and we looked at power density, and the only difference, for today's discussion so that we don't get down into the weeds, the only difference is that power density takes into account the conductivity of that tissue, because remember, the conductivity of a tissue, gray matter or white matter, is going to be different than a fluid-like CSF.

Dr. Matthew Ballo: And what we showed that was higher tumor treating field intensity, over one volt, improved overall survival. And 1.1 was the cutoff for the improved overall survival, for the power density. Remember, the only difference being that field intensity is more of a geometric relationship between these electrodes, whereas the power density takes into account the conductivity or the tissue density, okay? So, but for really the important thing, this is proof of principle that the patients that wore the device, we're only looking at patients who wore the device, patients who wore the device and had a higher dose to their tumor bed, lived longer. And again, to the radiation oncologists in the audience, that should be very exciting.

Dr. Matthew Ballo: And then, of course, you want to say, you want to make sure that that was controlled. We controlled for compliance. You don't want the people who got the highest dose to also be the people who wore it the most. So, this is controlled for compliance. So, these are independent. The intensity through the tumor bed independently increases overall survival. And then you would ask the question, okay, can we subgroup these patients into groups, where the people who wore the device the longest and had the highest dose through their tumor bed, they should live the longest. And the people who didn't use the device very often and had the lowest dose through their tumor bed, they should have the lowest overall survival. And that's exactly what turned out to be true, is that you can see, the bottom lines are the people who wore the device less had a lower dose through their tumor beds. The higher lines are the people who wore the device the longest and also had the highest dose.

Dr. Matthew Ballo: And this is just another way of looking at that same data. If you look at the Temozolomide alone, it was 16 months. The people who had the low energy, 21 months. These are looking at median survivals. And as you look at the higher energy group, and you look at those who were at less than 18 hours a day, 18 to 20, 20 to 24 hours, you see a clear improvement in the median survival. This is proof of principle. You can argue about the trial, you can ask questions about how it was done in specifics, but when you start to see things like dose improving overall survival, it gets harder and harder to criticize.

Dr. Matthew Ballo: At West Cancer Center, we have basically, we have integrated tumor treating fields into our practice. It is an option for patients, just like surgery is an option, just like radiation is an option, just like chemotherapy is an option. So, we don't say we're going to recommend that you have surgery, chemotherapy, and radiation therapy, and then, oh, by the way, you can also consider this other therapy. No, this is the standard of care. This is the institutional and the national standard of care, supported by the literature, supported by the data, supported by the NCCN. So, we have worked this into our clinic where the neurosurgeons talk about doing it, the radiation oncologists talk about doing it during the radiation therapy, preparing patients for their care. Just like we prepare them for adjuvant systemic therapy, we prepare them for the use of the device.

Dr. Matthew Ballo: One last thing I wanted to talk about was, “How confident are you that there are no significant evidence gaps that may impact positive health outcomes in the Medicare-eligible population?” One more thing I think that is very important to mention is that, during the trial, a quality of life was a predefined secondary endpoint in EF-14. They use the quality of life C30 and the BN20 questionnaires. Again, remember my gut told me, you've got this patient in a wheelchair, elderly, maybe not going to benefit. Well, that's been proven wrong. There is a benefit. There is an improvement in overall survival, but okay wait, maybe their last five months, four months, their quality life is going to be terrible. They won't be able to go out to eat, they won't be able to interact with their family, they won't be able to go out and garden, travel. But the reality is, they can.

Dr. Matthew Ballo: When we looked at deterioration-free survival, again, there was an actually an improvement in the patients that wore the device. They maintained their quality of life longer by using the device. So, I was proven wrong that these patients can interact, and that their quality of life is actually excellent.

Dr. Matthew Ballo: Okay, thank you very much.

Bill Doyle: So, I'll pick it back up just to conclude the review of the scientific evidence and then Steve will come up and give you the patient experience.

Bill Doyle: One of the things that I mentioned earlier on, but I wanted to provide the exact data that we have. Again, if we go before 2014, an emerging body of evidence, but by 2018, over 132 peer-reviewed publications of the clinical data and preclinical data of TT fields in the Medline database.

Robert Hoover: And then finally, as a summary chart here, why we assert that TT fields, while not used for every patient, has in fact achieved general acceptance in the medical community. First of all, the key numbers for the EF-14 clinical trial, a 0.63 hazard ratio for PFS and OS, and a p value of 0.0001, so highly significant data. Today, as I mentioned, 40% of the eligible patients in the country receive a prescription. We have achieved the NCCN category one listing. There are over 1100 prescribers, and recall too, this is a relatively fortunately rare disease, but 1100 prescribers throughout the country, 59 of the 62 NCI-designated cancer centers are prescribing, and all Americans who are privately insured are currently covered for this therapy. With that, as I introduced Steve earlier, Steve was a Senior Vice President at Siemens Electric Power Division, was working and continued to work while receiving Optune® therapy, and we wanted him to provide his perspective to the CAC today.

Steve W: Okay, first thing I did wrong is I got my cord in the wrong place. I'm not really that tall.

Steve W: Handsome dude, isn't he?

Steve W: Okay. Good morning, everyone. Thank you for having me. I'd like to thank the CAC panel and Novocure for the opportunity to share my story of living with GBM and thriving with Optune®. I hope that my experience, along with that of many others, will convince you that Optune® is a therapy that has already extended the lives of people, and at the same time, given them a good quality of life. Before I begin, I'd like to acknowledge my fellow warriors and their caregivers that are in the audience and that are listening online and that will, in the future, see this presentation. In my opinion, you are all warriors. You're my heroes. And I bless you for all the things that you've been through, and I wish you good luck.

Steve W: And personally, I'd like to thank you for finding the strength to lend your voice to this discussion is so critically important to the GBM and Optune® community. For those on the panel, I wish you had the opportunity to speak to some of these individuals. I wish you could get their unbiased perspective on what it's like to live with GBM. Unfortunately, there's only a few people in the audience. I know that some of you probably have had the chance to talk to some Optune® people, but I'm going to just go ahead and give you my view of life and hopefully that will correlate with some of the things that you've heard before.

Steve W: So, to help you get started, I'm going to tell you about myself. I'm a 60-year-old optimist. The glass is almost always half-full for me. I truly believe this is a trait is one of the reasons why I'm able to be here today. As Bill said, I retired a few years ago from a senior position in a global company so that I could fight my battle with GBM and spend more time with my family and friends. The challenge for me at the time was that I was not eligible to retire. What made things even more interesting was that my job required me to be in Europe, Asia, and the Middle East, but being the engineering optimist that I was, I was convinced that, myself, that I could still do my job, get to my early retirement date, and still have some time to battle my disease and have some fun. As you will hear, I've been incredibly fortunate thus far.

Steve W: My battle with GBM began six hours before I was scheduled to get on a flight to Shanghai. Earlier that day, I noticed that I was having some problems controlling my left foot. I didn't think much about it until, later in the day, my wife found me lying in the middle of our driveway. Suffice it to say, rather than getting on a plane to China, my wife decided I needed to get in a car to get an MRI. The MRI results indicated that I had a golf ball-sized mass in my right parietal lobe that was potentially glioblastoma multiforme. I didn't know what that meant, but it sure didn't sound very good. The few things that I remember from the first meeting with my doctor's visit was being told that there was no known cure for GBM. I sure didn't like hearing that. I was then told that if I did nothing, statistically, my chances of living past 14 months were very low. That didn't sound good either. To top it off, they said that if I had something called SOC, I had a less than 5% chance of living five years. I sure didn't like what I was hearing.

Steve W: So, at that moment, I committed myself to finding a way to beat the odds. I made it through surgery, radiation, and chemo, with no real issues, other than I was bald and I look like the Goodyear blimp. But I still went on and completed my radiation and chemo, and I continued to work throughout that time. In the evenings, I started to do research on what else could be done to beat the odds. I learned there were some really interesting research being done, and that some of it was showing promising early results. Unfortunately, nothing appeared to be close to being declared a cure. I decided I wasn't going to sit around and waste whatever time I had remaining. I started looking for clinical trials that hopefully would extend my life.

Steve W: I used the following criteria to evaluate my options: First, the trial had to have a large number of participants to statistically support the conclusions. Next, I wanted it to be innovative, partially because I'm an engineer. It also couldn't prevent me from trying other treatments. And most importantly, it had to give me a quality of life, if possible. After seeking a second opinion and discussing the results of my evaluation with my neuro-oncologists, we just concluded that I should enter the Optune® EF-14 clinical trial for newly diagnosed GBM cancers. I was placed, unfortunately, in the control arm with Temozolomide, also known as TMZ, but eventually crossed over to wearing the device. I've worn Optune® continuously since that time. I'm no longer on TMZ, I have not participated in any other trials, and most importantly, I've remained progression-free. That's pretty good, isn't it? Come on, somebody say yes. You don't hear that too often for people like me.

Steve W: Thus far, Optune® has met all my expectations. While wearing Optune® for at least 22 hours a day, I worked for a year and a half until I hit my retirement date. During that time, I was able to perform all my duties and to go to all the places I needed to be. In addition, I was able to do the things I enjoyed. With the consent of my doctors, I exercise regularly, I pursue my hobbies, I volunteer for various causes, and I travel throughout the world. Last year, I was able to trek around Alaska for two weeks with my family and friends. During the entire adventure, I wore Optune® on my back. I've learned of many Optuners, as we call ourselves, that are also doing incredible things, like running triathlons, playing in jazz bands, and going to exotic places.

Steve W: I know everyone's situation is different, and therefore I always recommend they consult with their doctors before they decide what they can and cannot do. I know there are some people that have concerns about shaving their heads, skin irritation, usage time of 18 hours a day, having to wear a backpack, and worrying about what others think when they see wires coming out of your head. These concerns are real, but I found that, with the help of caregivers, Novocure's device support specialists, and the Optune® community, most of these problems can be overcome, or at the very least, become more manageable. It hasn't always been easy. I dealt with many of these challenges myself, but for me, I consider them a very small price to pay for the potential benefit.

Steve W: As an engineer and a businessman who likes to make fact-based decisions, I have to admit, I don't understand what more is needed for Optune® to receive the Medicare seal of approval. We've already heard, that based on two extensive clinical trials, that Optune® was approved by the FDA several years ago. This eventually led to the NCCN declaring it part of the standard of care for GBM. We've also heard that the majority of insurance providers have been, look at that, I've extended, gone past my time. Make it easy here. You get to see it in action. We've also heard that insurance providers had been covering Optune® for some time. Based on these facts, many physicians have already prescribed Optune® to thousands of patients. As a result, many are showing measurable improvements in their overall survival with minimal side effects. To me, there already appears to be an overwhelming amount of information available to make a fact-based decision.

Steve W: One thing I've learned as an engineer was that when proposing a solution to a complex problem, occasionally, someone would question the results and ask for more data. In these situations, I found that if I'd done my homework and demonstrated that the risks were understood and manageable, then typically, there wasn't a need to do any additional reviews or studies. In the case of Optune®, it appears that the FDA, the NCCN, most insurance providers, and a large number of physicians believe that Novocure has done its homework.

Steve W: My hope today is that the CAC panel will come to the same conclusion. I believe that my experience, along with that of other Optune® users, demonstrates that there is a potential benefit, a potential for patients to have in meaningful improvement in their overall survival, while still having a good quality of life. For most of us diagnosed with GBM, we consider the opportunity to live one more day a blessing. Please help us make that happen.

Steve W: Thank you again for allowing me to tell my story, and for celebrating with me my five-year and two-day anniversary of living with GBM without a recurrence. Thank you.

Bill Doyle: So, that concludes Novocure's presentation to the CAC today.