



Canada's Drug and
Health Technology Agency

CADTH Health Technology Review

Optune (NovoTTF-200A)

Patient, Caregiver, and Clinician Input

Sponsor: Novocure Canada Inc.

Therapeutic area: Supratentorial glioblastoma multiforme

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Report Length:	32 Pages



Feedback Received on Optune

Patient input was received from the Brain Tumour Foundation of Canada. Information was gathered via online surveys and videoconference interviews conducted in 2023. In total, 339 responses were received for the online surveys (including 259 caregivers and 80 patients) and 10 interviews were conducted (with 6 patients and 4 caregivers, all of whom had experience with Optune). The majority of survey respondents were from Canada (> 94%). Patients with glioblastoma multiforme (GBM) reported experiencing a wide range of symptoms, including headaches, cognitive changes, changes in behaviour, weakness or problems with arms and legs, seizures, nausea, and problems seeing, all of which had a significant impact on their emotional and psychological well-being. Most respondents indicated that they or their loved ones had undergone surgery (88%) or radiation therapy (93%) for glioblastoma. It was noted that while these interventions helped decrease the tumour size or slow progression, effects were often short-term and associated with side effects. Input from the 10 individuals who had experience with Optune (plus temozolomide) indicated that Optune resulted in clear MRI results, increased survival, and helped them resume several daily activities. Scalp irritation and dermatitis were the primarily reported negative side effects associated with Optune treatment, with a few mentions of low blood platelet count, nausea, constipation, and tiredness. Overall, most individuals with Optune experience noted that they would recommend that the treatment be made accessible to people living with GBM.

Clinical input was received from several oncologists in Canada who treat patients with newly diagnosed GBM. Clinical input noted that current treatment of GBM requires a multidisciplinary approach, in which surgery is generally followed by postoperative radiotherapy with concurrent temozolomide, and after which maintenance temozolomide is given for a minimum of 6 months. The primary goal of therapy is to prolong life and progression-free survival (PFS) with minimal adverse events (AEs) while maximizing patients' quality of life (QoL). Clinical input further stated that no new treatment options for newly diagnosed GBM have been introduced since 2005, and currently available treatments continue to have a poor prognosis. Based on the EF-14 trial, clinicians indicated that outcomes used to assess treatment response would align with those in the EF-14 trial (i.e., PFS and overall survival [OS]). Factors relevant to health-related quality of life (HRQoL), neurocognitive functioning, and treatment-related cytotoxicity should be used to determine treatment discontinuation. Lastly, clinical input indicated that tumour-treating field (TTField) treatment requires no additional outpatient services (such as infusion sites).

No drug plan input was received for this review.

The original feedback that was provided to CADTH is presented subsequently.

Patient Input

Name of Patient Group: Brain Tumour Foundation of Canada (BTFC)

Author of Submission: [REDACTED]

1. About Your Patient Group

Founded in 1982, [Brain Tumour Foundation of Canada](#) (BTFC) is a charitable organization registered with the Canada Revenue Agency and Revenu Québec, that helps Canadians affected by a brain tumour through advocacy, support, education, information and funding of research. BTFC advocates federally, provincially, and locally for better government support and access within the healthcare system for people living with brain tumours. We have a nationwide support network that includes both in-person and online groups and have worked with Dr. Faith Davis, of the University of Alberta, to launch the national [Brain Tumour Registry of Canada](#).

2. Information Gathering

The information contained in this submission was gathered by Brain Tumour Foundation of Canada (BTFC) through online surveys distributed in French and English. In addition, 10 people - six patients and four caregivers - were interviewed in English and French regarding their experiences with Optune (NovoTTF-200A) and its impact on their lives. All data was contributed anonymously.

Responses to the online surveys were collected between May 10 and May 24, 2023, and videoconference interviews were also conducted during that timeframe, with the final interview taking place on July 31, 2023. Survey respondents were recruited by BTFC through email, social media, and other online platforms. The following populations were invited to take part: people living with glioblastoma ("patients") and those who are or were caregivers and/or loved ones of people living with glioblastoma ("caregivers").

A total of 339 patients and caregivers responded to the English (n=227) and French (n=112) online surveys. Most (n=259) were caregivers, and the remainder (n=80) were patients. Around 40% of the respondents were between 35 and 54 years of age, and 48% were between the ages of 55 and 74. All of the patients who responded to the survey were adults.

Majority of respondents were from Canada (>94%). A small number of responses were received from France, US, Germany, Algeria, and the Republic of Guinea.

Among the respondents affected by glioblastoma, approximately 80% reported they or their loved one received a diagnosis more than one year ago. Out of this subset, almost 49% received a diagnosis more than three years ago.

3. Disease Experience

Glioblastoma is the most common and aggressive malignant primary brain tumour. The tumours start as a growth of cells in the brain or spinal cord, quickly invading and destroying healthy tissue. The tumours contain various cell types, the most common being astrocytes that support nerve cells.

Glioblastoma accounts for 12-15% of all intracranial tumours and 50-60% of astrocytic tumours. It can manifest at any age, but mostly affect adults between 45 and 75 years of age. According to the Brain Tumour Registry of Canada, the incidence of glioblastoma is 4 per 100,000 people in Canada.

Glioblastoma moves with devastating speed. The median survival rate for adults is only 14.6 months – and for those who do not receive treatment, that timeline significantly decreases to only four months.

Symptoms:

Patients with glioblastoma experience a wide range of symptoms. Some of the most commonly reported symptoms from survey respondents included headaches, cognitive changes (changes in memory and concentration), changes in behaviour, weakness or problems with arms and legs, seizures, nausea, and problems with seeing. Several survey respondents also highlighted trouble with speech.

When asked about symptoms that posed the biggest challenge, **patient respondents** said:

- *« Rapidité de la dégradation de ses fonctions neurologiques. »*
- *“Memory and concentration issues. These things sometimes make it difficult to complete everyday tasks and I have yet to return to work due to my poor short-term memory and issues with word recall.”*
- *“Chronic fatigue and being tired easily makes it very hard to do day to day activities and keeps me from going back to work.”*
- *“The dizziness affects balance and therefore EVERYTHING.”*
- *“Seizures (are most challenging as they are) totally unpredictable, therefore a significant safety concern...She (the patient) lost mobility and ended up in a wheelchair, which limited her ability and desire to leave the house. She also lost cognitive function, which upset her quite a bit, as she had always been very clever and independent*

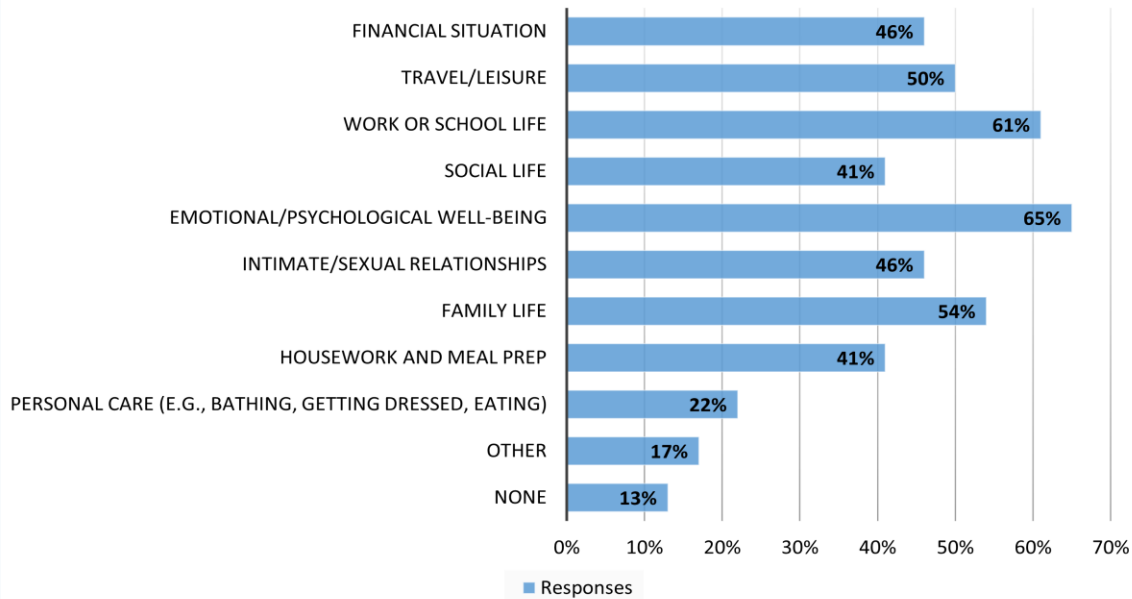
Disease Impact:

The impact of glioblastoma was said to be very pervasive, especially on **patients'** emotional and psychological well-being.

Patients indicated that they commonly rely on equipment such as, walkers, bed rails and canes. Other assistive devices and supports used by respondents included, phone apps, service animals, memory aids, ankle braces, neck brace, restraints, tub transfer bench, Hoyer lift, ramp, walking poles, bathroom rails, shower seat, incontinence diapers, Prism glasses (for homonymous hemianopia), and toilet seat risers. Emotional support from family, friends and caregivers was also referenced as critically important to people living with glioblastoma.

Approximately 21% of **patients** reported they did not use any assistive devices, equipment, or aids to manage symptoms and/or support their daily activities.

How does having glioblastoma affect your daily life? (Choose all that apply)



When asked to describe in their own words how their daily lives and quality of life have been impacted by glioblastoma, **patients** said:

- “I was stripped of my independence...”
- “(I) Can't do anything in a normal way.”
- « Je ne peux plus travailler. Je suis rendu très lent dans toutes mes actions. »
- “I have a severely decreased quality of life, and I rely on what seems like fugacious hope to make me feel worthy of another day in this dismal prison. I don't feel in control of my own fate.”
- “[My quality of life] has been quite negatively affected. My mental health has been quite detrimentally impacted, and my neurological deficiencies have diminished my self esteem. Frankly, I feel like I'm just waiting to die, which has been an awful way to live.”

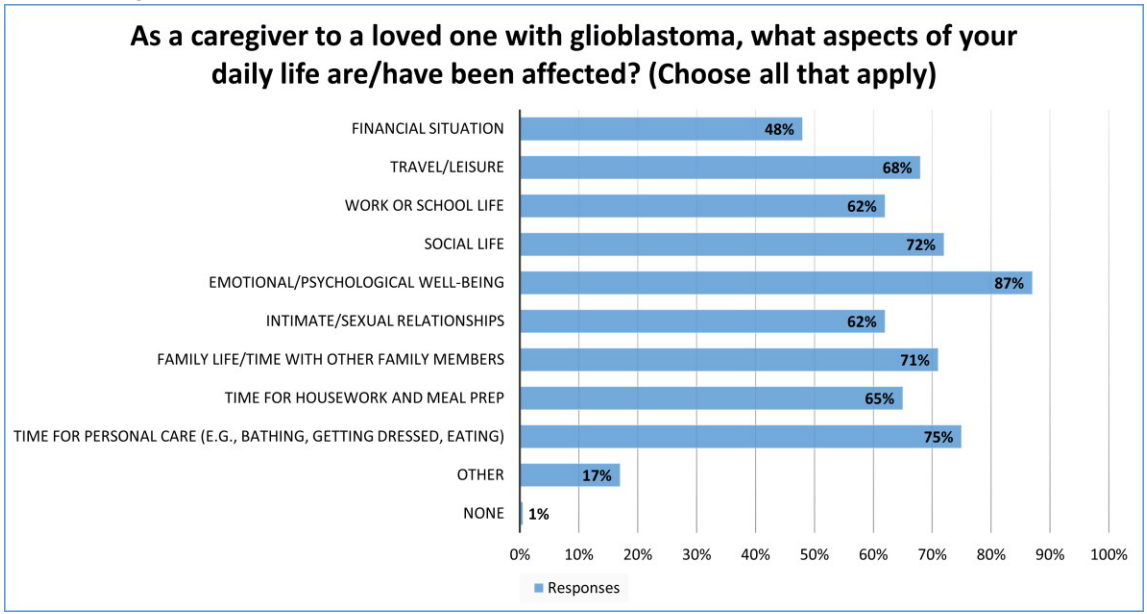
Impact on patients' loved ones:

When speaking about the affect their disease had on family and friends, **patient** respondents reflected on the psychological strain experienced by their caretakers. For example, one patient shared, “It's caused a huge amount of worry/anxiety to my family and loved ones...especially because it seems like long-term treatments are not definitive and I will always be on the lookout for tumour growth.” Another patient said, “My wife had to step up in a caregiver role for me... This has also had a severe impact on her mental health. My children are young, but they certainly have been impacted by my inability to be as active with them and to remember things...”

From a **caregiver** perspective, glioblastoma has negatively impacted many areas of their lives, including emotional and psychological well-being, time for personal care, social life, family life and time with other family members. Less than 1% of respondents reported that glioblastoma had no impact on their daily lives.

Several **caregiver** respondents mentioned feeling intense anxiety, a feeling of loss, and being overwhelmed, including experiencing depression. A number of survey respondents shared that they had lost their independence and ability to maintain their own life as they had become full-time caregivers. **Caregivers** also reported an impact on their work, as they had to reduce their hours in order to provide the level of caregiving needed by their loved one.

As **one caregiver** said: *“I no longer have the life I had before this diagnosis. It is all consuming.”*



When asked to describe in their own words how their daily lives and quality of life have been affected by providing care for someone living with glioblastoma, **caregivers** said:

- *“It was the worst. Every day watching my wife deteriorate while still trying to maintain happiness and hope was devastating. Alarm at 6am for meds and then non-stop all day...It was debilitating.”*
- *“Worry and anxiety are constant along with incredible sadness watching your child experience brain cancer...In the last couple months of our son’s life, it required both my husband and myself to look after him as he gradually lost all physical capacity. It was and is heartbreaking.”*
- *“There are no aspects of our daily life that have not been affected by glioblastoma... My mental health has suffered, both from being a caregiver and also the anticipatory grief that my child and I will lose him in the near future.”*
- *“Traumatized, unsupported, and frustrated... I felt so underprepared to be a caregiver and I all I wanted to do was provide the best for my mother and enjoy what time we had left. The lack of support and poor quality of life made it impossible to manage through daily.”*

4. Experiences With Currently Available Treatments

Patients and caregivers were asked about their experience with current standards of care including surgery, radiation therapy, temozolomide, bevacizumab and complimentary therapies.

Surgery:

Eighty-eight per cent of respondents indicated they/their loved ones had undergone surgery as an intervention for glioblastoma. While patients shared that the surgery removed or reduced the size of the tumour and had extended their lives, several indicated that its side effects had an adverse impact on the daily-life or only provided relief for a short period of time.

Common post-surgery side effects included numbness, loss of speech, aphasia, seizures, and loss of strength.

When asked **how surgery helped** them or their loved ones, respondents said:

- *“It relieved the effects of hydrocephalus in terms of the intensity of headaches. Surgery also made the majority of my tumour accessible, and the initial resection accounted for about 80% for the first surgery.”*
- *“It has eliminated any speech impediment and has resulted in a sustained survival.”*
- *« Retrait d'environ 95% de la tumeur combiné aux autres traitements m'ont permis d'être fonctionnelle pendant environ 8 mois. Récidive par la suite. »*
- *“It helped to lengthen life and slightly diminish tumour side effects.”*
- *“When my loved one was admitted to the hospital, he had severe swelling in his brain. He would've died very quickly without surgery. He was becoming very quiet and losing his ability to walk. He kept saying "something isn't right in my head." Already after starting dexamethasone there was massive improvements in his symptoms. And as he healed from his surgery his symptoms improved even more. He became much more talkative and had less difficulties finding words. His concentration and cognitive functioning improved.”*

Regarding **problems and complications related to surgery**, respondents shared:

- *“Only helped for a short time (month or two). Then became much worse.”*
- *“It removed the tumor, but greatly decreased her quality of life. She woke up from surgery seizing and with moderate-severe aphasia. Luckily now it has been downgraded to mild aphasia. She has never regained her strength and now spends her days sitting in her chair. A huge change from her active lifestyle prior to surgery.”*
- *“Removed 80 % of tumour but left me with a TBI (traumatic brain injury).”*
- *“(There was) Loss of mobility on his right side. Loss of speech. Infection and also requiring a second surgery to place a shunt.”*

When asked how their **daily life has been/was affected as a caregiver** to a loved one with glioblastoma who had undergone **surgery**, caregivers shared:

- *“There was a shift in shared responsibilities, i.e. I became responsible for pretty much everything.”*
- *“Surgery was seen as an opportunity to buy time for a treatment. However, it was well understood that prognosis for long term survival after surgery was negligible. Of course, this only increased the stress, anxiety, and feelings of hopelessness that my loved one was going to die most likely within a year.”*
- *“Exhausted, worried, endless research to ensure I am not missing anything. Helping her with her daily activities while maintaining our own home, a full-time job, an aging parent. I wonder every minute of everyday how she is doing.”*
- *« Beaucoup d'inquiétude et de l'incertitude concernant notre futur ensemble et pour la santé de mon conjoint. Nous sommes nouvellement retraités et avons beaucoup de plans pour notre retraite. On a dû annuler un voyage qui était prévu. De plus, nous avons dû trouver un logement rapidement et déménager (3 fois en 6 mois) à Ottawa afin que mon conjoint puisse recevoir ses traitements (ultérieurs) à l'hôpital d'Ottawa »*

Radiation Therapy:

Approximately 93% of the respondents cited that they/their loved ones had experience with radiation therapy. Many indicated ambivalence about the impact of radiation therapy and shared they were uncertain about its effectiveness. Loss of memory and fatigue stood out as the most common side effects. And while it was shared that radiation therapy often helped to decrease the

size of the tumour or slow its progression, the effects were short-term – the tumour often returns or continues to grow post-radiation.

When asked **how radiation therapy helped** them or their loved ones, respondents said:

- *“Seemed to have shrunk the tumour temporarily.”*
- *“Helped to keep the tumour from growing rapidly.”*
- *“It did shrink the tumour and allowed her to eat normally until it grew back. With physiotherapy, she was able to gain some strength back in her arms and legs.”*
- *« État est resté stable, tumeur était contrôlée. »*

Regarding **problems and complications related to radiation therapy**, respondents shared:

- *“He (the patient) was absolutely exhausted and needed to sleep the rest of the day after radiation. We noticed more changes in him and his mobility after radiation. He became weaker.”*
- *“Radiation left him (the patient) with word finding difficulties and required steroids, Dexamethasone, which altered his personality.”*
- *“Cardiac arrest and an end to treatment before a full first round was done.”*
- *“It made him very ill. Continually the radiation caused inflammation in his brain, blocked the EVT (endoscopic ventriculostomy), and made him lethargic with headaches and vomiting. Twice he went into a stupor like state with vomiting and I had to rush him to the ER at the hospital he was being treated at in Toronto (from Niagara)...”*

When asked about **how their daily life has been/was affected as a caregiver** to a loved one with glioblastoma who received **radiation therapy**, caregivers shared:

- *“I scheduled my life so that I made sure I was with him for every radiation treatment.”*
- *“I had to leave my children behind in the care of a family member while he was undergoing radiation treatment as he needed to stay in a patient lodge close to treatment. He needed support for the last 4 of the 6 weeks of his treatment.”*
- *“Every aspect was changed. I put my life on hold for a year and a half. I moved into her home in another city. Life became about caring with little time for me. I became part PSW having to help with activities of daily living.”*
- *« Nous habitons à une heure de l'hôpital donc le reconduire tous les jours pour ses rendez-vous occupait la majorité de mon temps. De plus, les rendez-vous n'étaient pas à la même heure donc il était impossible d'avoir une routine. »*

Temozolomide (Temodal):

Over 80% of respondents indicated experience with temozolomide, a type of chemotherapy used to treat glioblastoma. Around 21% of the respondents shared they often faced barriers accessing temozolomide due to a lack of drug plan coverage or out-of-pocket costs. Challenges associated with picking up or having the therapy delivered and taking it on time were also identified as issues around access.

Respondents noted difficulties taking temozolomide including swallowing or keeping it down, as well as ensuring precision of dosage. Common side effects included nausea, dizziness, tiredness, and a negative impact on blood count. Around 44% of the respondents reported no difficulty in taking this treatment.

When asked about any benefits experienced as a result of taking temozolomide, several respondents shared that it helped reduce the size of the tumour and stabilized its growth, sometimes combined with other therapies. However, most **caregivers** were

unsure about any benefits from receiving this treatment and observed several side effects that altered the patient's overall quality of life.

On **how temozolomide helped** them or their loved ones, respondents said:

- *"It helped my husband by giving him a better chance to survive as it removed the rest of the tumour."*
- *"Reduced seizure frequency."*
- *"His cancer hasn't returned so it would seem it has helped significantly."*
- *"Likely eradicated whatever remained after surgery and radiation."*

Regarding **problems and complications related to temozolomide**, respondents shared:

- *"Low blood counts, negative impacts on immune system leading to me contracting PJP Pneumonia (Pneumocystis jiroveci pneumonia)."*
- *"Body rash at start of treatment and mitigated with antihistamines."*
- *"Immunocompromised my mom in a bad way."*
- *"Side effects from temozolomide were horrific. His (the patient's) blood counts plummeted, which prevented him from continuing treatment and eliminated many other treatment options."*
- *"Nausea, weakness, tiredness, lack of appetite, memory/word finding problems."*
- *"Due to very low platelet and white blood count numbers, he was hospitalized in reverse isolation for months. This resulted in many days spent at the hospital, so keeping up with daily life and caregiving remains a challenging balance."*

When asked about **how their daily life has been/was affected as a caregiver** to a loved one with glioblastoma who received temozolomide, caregivers shared:

- *"It was tough staying regimented for evening dosage and it was pretty scary dealing with "electrified pills" that would stay stuck with static to the wall of the pill cup."*
- *"During treatment, it has been difficult to manage my husband's nausea. I have needed to work with his medical team to manage several medications with different timings and dosages. Dealing with the insurance companies to ensure coverage has also been very stressful."*
- *"Exhausted from trying to find something that would help my boy (the patient) to not have nausea and vomiting. Feeling of hopelessness that there was nothing I could do to change it."*
- *"You have to be there for them 24/7."*
- *"His extreme fatigue put our life in limbo, (experienced) worry."*

Bevacizumab (Avastin):

Over 19% of the respondents shared they or their loved ones had experience with bevacizumab, a type of targeted therapy called an angiogenesis inhibitor. An angiogenesis inhibitor is a monoclonal antibody that works by blocking the growth of blood vessels needed to support tumour growth and is used to treat glioblastoma.

Fifty per cent of the respondents shared that they experienced difficulties accessing or taking bevacizumab, including managing out-of-pocket costs or qualifying for drug plan funding. One caregiver noted, *"We are in the process of trying to get the coverage. It has been in the works for two weeks, but we still do not know if he will be eligible. If he does get it, we will have to drive the 2.5 hours for the infusion."* The remaining 50% of the respondents reported no difficulty in accessing or taking this treatment.

When asked about any benefits experienced as a result of taking bevacizumab, several respondents indicated that it “bought them some time” although several felt that it did not make a notable difference. Among side effects shared, several respondents noted a drop in patients’ platelet counts.

On **how bevacizumab helped** them or their loved ones, caregivers said:

- *“Yes! My husband (the patient) had 28 infusions. He tolerated them very well and I believe they helped him.”*
- *“It gave him (the patient) a few months of quality living and a brief remission.”*
- *« Les effets ne se sont pas fait sentir. »*

Regarding **problems and complications related to bevacizumab**, both patient and caregiver respondents shared:

- *“Weakness in muscles, difficulty walking, blood clot, abscess requiring urgent surgery, tiredness, skin rash and lesions on his (the patient’s) back and front.”*
- *“Severe drop in platelet count; her infusions had to be postponed numerous times and three times she ended up in ER for blood transfusions.”*

When asked about **how their daily life has been/was affected as a caregiver** to a loved one with glioblastoma who received bevacizumab, caregivers shared:

- *“I was taking care of him (the patient) daily, going to the clinic for Avastin and other medical appointments, ER, trying to figure out why he had all these symptoms.”*
- *“I took a leave from work and my degree to be his (the patient) caretaker. I took him to every treatment bi-monthly.”*

Complementary treatments/therapies:

Around 24% of the respondents shared that they had used complementary therapies including, natural products (43%), mind and body practices (40%), acupuncture (15%) and manual therapies (11%). Other complementary therapies cited included Reiki, music therapy, oral cannabis oil, cannabidiol, physiotherapy, Loco Regional Hyperthermia (LRHT), lymphatic massage, intravenous vitamin C, and counseling among others.

Some patients and caregivers mentioned participating in clinical trials for investigational therapies other than standard treatments directly available to them.

Several respondents indicated that alternative therapies helped to “ease the mind.”

On **how complementary treatments/therapies helped** them or their loved ones, respondents said:

- *“Reiki relaxed him (the patient). We did not have a helpful music therapist, but my husband joined a band to which he went to rehearsal every week for about 24 of the 30 months he lived with glioblastoma and that was tremendously helpful for his spirits, memory, and motivation”*
- *“Mindfulness meditation help reduce anxiety to some extent and nutritional supplements help to maintain strength and ability to remain active”*
- *“Kept her (the patient) grounded and living in the moment. Something else to focus on”*
- *“Definitely extended the health, and quality of life. Supported immune system”*
- *“Eased dealing with the diagnosis”*
- *“I am quite certain the combination of the above (multiple complimentary therapies) is what has kept my tumor from growing*

back, and have kept my symptoms to a minimum”

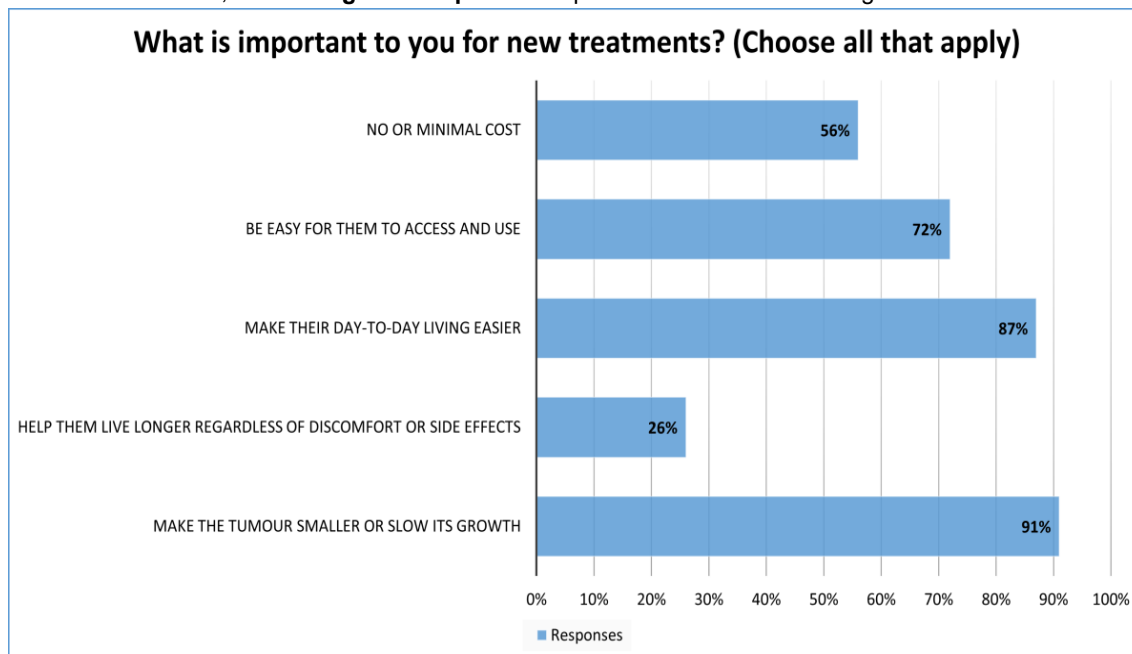
- “Using herbs and such I felt much better, the yoga helped me when I was stressing, and the acupuncture helped with some of aches I was having as I recovered”
- “It’s helped me get the nutrition needed for my body but also my mentality”

When asked about **how their daily life has been/was affected as a caregiver to a loved one with glioblastoma who is/was using complementary therapies**, caregivers shared:

- “It was disheartening as she was grasping on to anything she could to treat herself, because the chemo/radiation didn’t work.”
- “May have given a feeling of hope.”
- “It was hard to get our hopes up that something might help just to have them dashed when it didn’t.”
- “It has been a slight relief.”
- “I eventually became a naturopathic doctor I was so inspired by how well they treated my mom.”

5. Improved Outcomes

When asked what improvements they would like to see in a new treatment for glioblastoma that are not achieved in currently available treatments, most **caregiver and patient** respondents mentioned making the tumour smaller or slowing its growth.



If the desired improvements they hoped for in a new treatment were achieved, **patients** said:

- “I could live my life without the constant paralysis of fear of death and move on with reassurance I will have ample time to enjoy and experience things and build my career, find true love, and achieve all my life goals etc.”
- “I would be able to take back some of the daily things to help my wife again. Spend time with my kids running around,

building things...

- « *Vivre ma retraite pleinement avec ma famille.* »
- *“I would go back to work, be able to go on trips, feel more normal / independent which is how I was before getting diagnosed.”*

When asked about the improvements that **caregivers** would like to see in a new treatment for glioblastoma, it is not surprising that “more time with their loved one” stood out as a common response, along with a desire to see their loved ones retain their functions as long as possible to have a better quality of life.

If the desired improvements they hoped for in a new treatment were achieved, **caregivers** said the result would be:

- *“Anything that eased day-to-day living would add to quality of life”*
- *“It would have given my son more hope. He could possibly go back to some of the sports he was missing. He would be happier and more outgoing instead of isolating.”*
- *“My wife was a very dynamic, active, independent woman. Losing all that was very hard on her, so anything that would have allowed her to maintain her autonomy longer would have been welcome.”*
- *“If the tumour growth could be stopped, slowed or if the tumour were to shrink, the side effects that he is suffering could diminish and he could resume some normal daily activities & regain control of a more normal life. He would be able to become independent again and perhaps even resume work.”*

6. Experience With Device Under Review

Of the **patients and caregivers** who shared their experience using Optune (with temozolomide), most received the device through compassionate use from the manufacturer. A small number of patients advocated to access the device through clinical trial participation, and one respondent mentioned accessing Optune through an insurance plan.

Regarding the sequencing of therapies for glioblastoma, patients (and caregivers) interviewed indicated that surgery was the first-line treatment recommended unless not possible due to the location of the tumour. Surgery was usually followed by medication(s) to manage post-operative symptoms, and then radiation therapy before starting chemotherapy. The patients interviewed went on to receive treatment with Optune in combination with temozolomide.

Respondents indicated that using Optune resulted in clear MRI results, increased their survival and helped them resume several daily activities. One caregiver said, *“My son used it for 2.5 years. His MRI results were consistent for 7 years or more. He surpassed the median life expectancy for GBM (glioblastoma). Others in the support group who did not use Optune passed long before my son.”* Another shared, *“My son was relatively well during his 2 years of treatment. Yes, he had side effects, but he was skating and playing hockey for part of this time. If he hadn’t had the hemorrhage and had this treatment earlier, he very well may have lived longer.”* Another caregiver said, *“He (my late son) used it for two and a half years. Through those two and a half years, the MRIs were always the same...in our minds that was proving that it was working. Nothing was progressing and he didn’t see a progression in the MRI until years later (the patient was not on Optune when the MRI changed)... so that was a fairly long period with no changes. I honestly thought he may have beaten this because every MRI was the same.”*

When asked about any negative impacts experienced while using Optune, most **patients and caregivers** mentioned scalp irritation and dermatitis. While a majority of **patients** experienced only skin-related issues, a few people (patients/caregivers) mentioned low blood platelet count, nausea, constipation, and tiredness.

In addition, while most patients reported that the weight of the device was not a notable concern for them, one patient using the first-generation Optune system (weighing approximately 6 pounds - ~2.7 kg) shared, “I find the battery pack a little bit cumbersome and heavy, so I don’t carry it around with me during the day (say) when I’m vacuuming or gardening.” The second-generation redesigned Optune system, currently available in Canada, weighs 2.7 pounds (~1.2 kg) which may be easier to use for some patients. A patient user survey conducted by Novocure suggested that patient satisfaction with the second-generation

Optune system is improved versus the first-generation system and supports a higher rate of treatment compliance.¹ Another caregiver shared, about his late son that he decided to stop using Optune because *“it did not suit his lifestyle...he liked to travel, and not that you cannot travel with it, it’s just cumbersome and he was used to being freewheeling.”*

¹ Kinzel, A., Ambrogi, M., Varshaver, M., & Kirson, E. D. (2019, January 29). Tumor treating fields for glioblastoma treatment: Patient satisfaction and compliance with the second-generation Optune® System. Clinical Medicine Insights Oncology. <https://pubmed.ncbi.nlm.nih.gov/30728735/>

One caregiver spoke to us at length about his late son’s experience with Optune, as compared to other treatments: *“Surgery is very intrusive, and we experienced a huge amount of stress because of the risks although my son didn’t have any real problems with the surgery. Following the 30 days of radiation, the fatigue was huge for my son. He developed thrush and had to get his molar removed because of a growth in his gum after radiation therapy. Chemo resulted in nausea and impacted his diet, and you could see how down he was during those periods. It’s a process that you have to learn to adapt to, because for those few days, you can’t do anything...so that’s like a week out of your month that you have to put aside and say that I’m gonna sleep during those...Optune is totally different. It is relatively pain free and it is the easy way because it’s a medical device, and what it impacts is your lifestyle. I guess in some manner your lifestyle now has to include shaving your head, putting the device on, and answering questions from people who see you in public and say, ‘what is that thing’, and he (his son) took to it really well. He became the guy that answers all the questions about this device on his head and so he was pretty happy with that. On the negative side, you have to have a caregiver to help you put the device on. Activities like taking a shower and swimming had to be planned in advance...My understanding is that now the new version of Optune is a little bit smaller and compact.”*

Another patient commented on her preference for Optune saying, *“It is a non-invasive therapy.”*

Almost all patients using Optune and caregivers of people on the treatment would recommend that it be made accessible to people living with glioblastoma. One caregiver noted, *“It is hope and has proven to increase the mean time for survival over the current standard of treatment (which hasn’t changed in a long time). Some might look at it and say yes but its only maybe 4 months. You will find that when you are faced with mortality, 4 good months is worth a lifetime.”* Another shared, *“If you have a diagnosis such as glioblastoma, anything that can help should be provided.”* In addition, another caregiver, speaking about whether Optune should be made accessible through public funding, said, *“I would say absolutely because this is a proven technology that is showing to extend people’s lives...the stats are there...Some people might say it’s only four months. Four months when you’re faced with the timeline that you’re going to die, four months could be a lot of time to you...and I think the biggest thing is it gives you hope... you’re doing something better than the average, better than the status quo...It gave us hope the whole time like this thing is keeping us alive and my son firmly believed that as well. He had his (personal) reasons for giving it up... but he had he had a lot of good years, a lot of very good years.”*

A patient using Optune who spoke to us shared that she was not able to have surgery but felt that the device was prolonging her life by keeping her condition stable. She said,

« Ils ne peuvent pas m’opérer ça fait qu’avec Optune ça ne progresse pas et tout va bien...Mes attentes, ce n’est pas de guérir à 100% parce que je le sais que c’est quelque chose qui ne sera peut-être pas possible, mais c’est au moins, peut-être, de garder ça stable, de faire en sorte que j’ai des années qui se rajoutent ... ».

A caregiver who lost her husband to glioblastoma told us that Optune gave the patient, and consequently the family, a degree of respite by gradually helping him regain his strength for a while which allowed him to spend quality time with his family before his passing. She said *« Cela (Optune) nous aura permis d’aller faire les sucres. C’était son rêve d’aller aux sucres avec la famille... Tous les voisins sont venus, nous avons fait de la tige, au soleil. »*

Another patient shared about his gradual adjustment to using Optune. He stated, « *La machine fait partie de ma vie, si je ne la porte pas je la cherche. Je me promène partout avec, puis c'est certain que ça été un ajustement, mais j'ai passé à travers des ajustements durant les deux dernières années, sinon je serai mort.* »

Patients using Optune and caregivers of people on the treatment resoundingly want to see it made accessible to those living with glioblastoma because it has given them hope, has allowed them more time with their families, caused minimal side effects compared to other treatments, and extended their lives beyond expectations. One patient said very simply, « *Moi, ça m'a redonné vie.* ». Another patient and father of three said, "Considering the existing stats and numbers (around Optune's impact), it definitely should be funded. How can you not give this opportunity to people? They should be given the opportunity to extend any time they get. The other part is that it provides people hope and a quality of life, because if you're wearing this device, you feel like you're a part of the process of healing and extending your life." A caregiver told us, "*It feels like you've been given a death sentence, and this is the only thing that you know of all the options that might give you a chance, and it's expensive, but if people are willing to (use this), how to deny that? It feels like you're just a sitting duck.*"

7. Companion Diagnostic Test

N/A

8. Anything Else?

Glioblastoma is the most common and one of the most aggressive forms of primary brain cancer. Glioblastoma's median survival rate for adults is 14.6 months, which can be devastating for patients and their loved ones. With treatment, people may survive longer. The average life expectancy with this disease is only four months for those who do not receive treatment.

Optune is the first new treatment for glioblastoma approved in Canada in over 12 years. It delivers TTFIELDS therapy to the region of the tumour and it is small and light, weighing only 2.7 pounds. This makes Optune wearable and portable, so continuous treatment can be received almost anywhere.

While answering the survey question about the impact of desirable treatment outcomes, a caregiver said, "*It (Optune) may have prolonged his life (the patient's) significantly, as I spoke to several people who had the Optune device during a trial in Canada 5 years ago and they are still alive.*" Another caregiver commented, "*(It's) a horrible disease with few advances in decades, something new MUST be done to help these patients and their families.*"

While sharing about how their loved one's daily life would change if a new treatment was able to provide desirable improvements and was accessible, a caregiver shared, "*It (an ideal new treatment) might allow him to move away from work as there would be less concern about the impending cost of treatments. This might let him transfer that energy to more positive contributions around the house and with family or doing things he enjoys. If he could manage day-to-day easier then he might be more open to being social.*"

Another caregiver shared "*Reducing the size of the tumour would allow our son to be more independent and therefore reduce caregiver requirements (and) covering or minimizing costs would be a major stress remover.*"

A caregiver and patient (spouses) shared that they are very hopeful about having access to this treatment sooner rather than later and want it to be made available to anybody living with glioblastoma. Currently, they do not have access to Optune and are trying hard to resolve this.

A deceased patient (whose father spoke to us) had been interviewed by a news outlet in 2018. At this interview, he had said, "*I am finding myself in a situation where I have this new tool in the form of me surviving this cancer that I wasn't supposed to survive. I figured I would use that tool and see what I can make of it.*" In another interview conducted in 2017, he said, "*For a while I was living day to day...and then eventually it went week to week, eventually it went to month to month. For the first time in a long time, I am looking year to year...It (Optune) allowed me to regain control over my life.*"

A patient and father of two disabled children who is currently using Optune said, *“if everything is continuing like now, where I just keep getting better and better, it’s somewhere I want to be...I know it before an MRI (if there is a change in my tumours)...and we haven’t had any of that, and knock on wood, things are looking up.”*

Patient Group Conflict of Interest Declaration

- To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

BTFC completed the submission independently with external support from EVERSANA.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

As noted above, BTFC completed the submission independently with external support from EVERSANA.

List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 1: Financial Disclosures

- Check Appropriate Dollar Range With an X. Add additional rows if necessary.

Company	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Novocure			X	
Acuitas Therapeutics			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: [REDACTED]

Position: [REDACTED]

Patient Group: Brain Tumour Foundation of Canada

Date: August 30, 2023

Clinician Input

Name of Clinician Group: Canadian oncologists who treat patients with newly diagnosed glioblastoma (ndGBM)

Author of Submission: [REDACTED]

1. About Your Clinician Group

We are a group of Canadian oncologists who treat patients with newly diagnosed glioblastoma (ndGBM). We represent the specialty from across the country in both academic and community settings and share the goals of improving the outcomes and quality of life of patients diagnosed with GBM.

2. Information Gathering

This submission was drafted by [REDACTED], one of the investigators of the randomized phase III trial investigating health-related quality of life, cognitive screening, and functional status of tumor treating fields (TTFields) with temozolomide (TMZ) compared to TMZ alone in newly diagnosed glioblastoma.

3. Current Treatments and Treatment Goals

Glioblastoma (GBM) is the most common primary central nervous system (CNS) cancer, representing approximately 48% of all cases. In 2021, approximately 945 Canadians were diagnosed with brain/CNS tumours, 81% of whom were aged 18 years and older. Treatment of GBM requires a multidisciplinary approach to optimize treatment outcomes. Surgery is typically followed by post-operative external-beam radiotherapy with concurrent TMZ. Following concurrent therapy, adjuvant TMZ is given for a minimum of 6 months. With this treatment, median survival is only 15 months and only 25% of patients can expect to live for 2 years. The goals of treatment are to prolong life and progression-free survival while minimizing adverse events due to toxicity and maximizing quality of life (QoL).

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Despite therapeutic advances for many other cancers, there have been no new treatment options for ndGBM since 2005. Due to their poor penetration, very few cytotoxic or immunotherapeutic agents have been effective in increasing survival. With such a poor prognosis, patients need additional, innovative treatment options.

5. Place in Therapy

5.1. How would the device under review fit into the current treatment paradigm?

Tumour Treating Fields (TTFields) using OPTUNE® represents a novel, innovative therapeutic option for patients with ndGBM. OPTUNE® is a portable and non-invasive device that provides continuous, loco-regional electric fields that disrupt cancer cell division at a specific frequency (100 to 300 kHz).

The TTFields are delivered through adhesive patches attached to the scalp (transducer arrays) connected to the OPTUNE® battery, which weighs about 1.2 kg and can be worn during patients' daily routine, including while they are asleep (minimum of 18 hours/day for optimal response).

EF-14 (NCT00916409) was a phase 3, randomized, open-label, active comparator trial that compared the efficacy and safety outcomes of ndGBM subjects treated with TTFields + TMZ to those treated with TMZ alone. The study enrolled 695 patients between July 2009 and November 2014 at 83 centers across the world. (1, 2) After completion of chemoradiotherapy, patients were randomized to receive maintenance treatment with either TTFields plus TMZ (n = 466) or TMZ alone (n = 229) and after 5 years of follow-up, statistically significant increases in progression-free survival (PFS) (6.7 versus 4.0 months, respectively P<0.001; HR 0.63 [95% CI 0.52 to 0.76]) and overall survival (OS) (20.9 versus 16 months respectively, P<0.001; HR 0.63 [95% CI 0.53 to 0.76]) were seen, all while maintaining QoL. The percentage of patients alive at 5 years was 13% (95% CI 9% to 18%) vs. 5% (95% CI 2% to 11%; P=0.004) in the respective treatment arms. (2) The treatment was well tolerated with the most common side effects including scalp irritation (redness and itchiness) and headache. (3)

5.2. Which patients would be best suited for treatment with the device under review? Which patients would be least suitable for treatment with the device under review?

Patients most likely to respond (i.e. to have prolonged PFS and OS) were those treated with TTFields in addition to maintenance TMZ chemotherapy following standard chemoradiation. In post-hoc analyses of the EF-14 trial (2), TTFields plus TMZ was associated with an increase in PFS and OS in all subgroups of patients and regardless of MGMT promoter methylation status.

5.3. What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

The outcomes used to assess treatment response align with those used in clinical trials and in standard clinical practice (i.e., PFS and OS).

5.4. What factors should be considered when deciding to discontinue treatment with the device under review?

Health-related QoL (HRQoL) and neurocognitive functioning should be monitored, as well as treatment-related cytotoxicity. HRQoL, cognitive, and functional status have not been shown to be adversely affected by the continuous use of TTFields. Patients treated with TTFields+TMZ reported concerns of "itchy skin". (3)

5.5. What settings are appropriate for treatment with Optune? Is a specialist required to diagnose, treat, and monitor patients who might receive Optune?

All patients with GBM must be treated in a specialized oncology service with all treatments prescribed by oncologists with expertise in GBM. Importantly, this treatment requires no additional outpatient services, such as infusion sites.

6. Additional Information

Although TTFields therapy was only approved in Canada in 2022, the Canadian Special Access Program (SAP) provided TTFields to 61 patients with GBM, 41 of whom were newly diagnosed. The author of this submission has patient in Calgary who was started treatment on the trial on in 2014 and stopped treatment in January 2023, well exceeding the survival prognosis for the vast majority of patients with GBM. Similar to the published data, TTFields was well tolerated over this time.

Further data will be provided by the TRIDENT trial (EF-32: trial <https://novocuretrials.com/cancer-clinical-trials/glioblastoma-clinical-trial-trident/>), an RCT investigating the safety and efficacy of TTFields from the OPTUNE® System together with concurrent radiation

and TMZ in newly diagnosed GBM patients. Enrollment is ongoing (expected N=950 patients) in in the US, Canada, Japan, and Europe.

References cited:

1. Stupp R, Taillibert S, Kanner AA, et al. Maintenance therapy with tumor-treating fields plus temozolomide vs temozolomide alone for glioblastoma: a randomized clinical trial. *JAMA*. 2015;314(23):2535-43.
2. Stupp R, Taillibert S, Kanner A, et al. Effect of tumor-treating fields plus maintenance temozolomide vs maintenance temozolomide alone on survival in patients with glioblastoma: a randomized clinical trial. *JAMA*. 2017;318(23):2306-16.
3. Zhu J-J, Demireva P, Kanner AA, et al. Health-related quality of life, cognitive screening, and functional status in a randomized phase III trial (EF-14) of tumor treating fields with temozolomide compared to temozolomide alone in newly diagnosed glioblastoma. *J Neurooncol* 2017;135(3):545-52.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH reimbursement review programs, all participants in the device review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the [Procedures for CADTH Drug Reimbursement Reviews](#) (section 6.3) for further details.

Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

- Editorial support was provided by a medical writer ([REDACTED]).

Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

- No

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.

Declaration for Clinician 1

Name: [REDACTED]

Position: [REDACTED]

Date: 27-07-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 2

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 3

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 4

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Oncology Education	X			

CADTH	X			
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Declaration for Clinician 5

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 6

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 6: Conflict of Interest Declaration for Clinician 6

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 7

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 7: Conflict of Interest Declaration for Clinician 7

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 8

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 8: Conflict of Interest Declaration for Clinician 8

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 9

Name: [REDACTED]

Position: [REDACTED]

Date: 14-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 9: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*
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Company	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Novocure			X	
AstraZeneca	X			
Roche	X			
Accuray	X			
Recordati Rare Diseases	X			
Kyowa Kirin	X			

Declaration for Clinician 10

Name: [REDACTED]

Position: [REDACTED]

Date: 15-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 10: Conflict of Interest Declaration for Clinician 10

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000

N/A				
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Declaration for Clinician 11

Name: [REDACTED]

Position: [REDACTED]

Date: 15-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 11: Conflict of Interest Declaration for Clinician 11

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Novocure		X		

Declaration for Clinician 12

Name: [REDACTED]

Position: [REDACTED]

Date: 15-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 12: Conflict of Interest Declaration for Clinician 12

	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Company				
N/A				

Declaration for Clinician 13

Name: [REDACTED]

Position: [REDACTED]

Date: 16-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 13: Conflict of Interest Declaration for Clinician 13

	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Company				
N/A				

Declaration for Clinician 14

Name: [REDACTED]

Position: [REDACTED]

Date: 17-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 14: Conflict of Interest Declaration for Clinician 14

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 15

Name: [REDACTED]

Position: [REDACTED]

Date: 17-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 15: Conflict of Interest Declaration for Clinician 15

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 16

Name: [REDACTED]

Position: [REDACTED]

Date: 17-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 16: Conflict of Interest Declaration for Clinician 16

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 17

Name: [REDACTED]

Position: [REDACTED]

Date: 19-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 17: Conflict of Interest Declaration for Clinician 17

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				

Declaration for Clinician 18

Name: [REDACTED]

Position: [REDACTED]

Date: 21-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 18: Conflict of Interest Declaration for Clinician 18

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000

N/A				
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Declaration for Clinician 19

Name: [REDACTED]

Position: [REDACTED]

Date: 22-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 19: Conflict of Interest Declaration for Clinician 19

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
Novocure	X			

Declaration for Clinician 20

Name: [REDACTED]

Position: [REDACTED]

Date: 29-08-2023

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 20: Conflict of Interest Declaration for Clinician 20

Company	Check appropriate dollar range*			
	\$0 to \$5,000	\$5,001 to \$10,000	\$10,001 to \$50,000	In excess of \$50,000
N/A				