

USC BRAIN TUMOR CENTER

Report

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SUMMER 2023

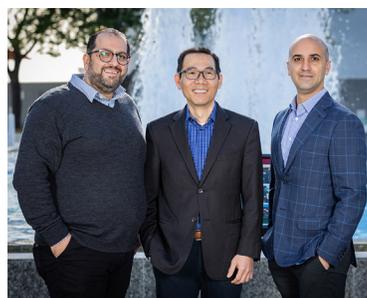
From the USC BTC Directors

At the USC Brain Tumor Center, we are committed to delivering the best care and support to all our patients and we are thrilled to share some exciting updates and news in this Summer 2023 Newsletter.

The USC Brain Tumor Center continues to rapidly grow, and we are delighted to introduce **Aram Modrek MD, PhD**, who has joined our Brain Tumor Center and the **Department of Radiation-Oncology**. Dr. Modrek brings with him a wealth of experience in the treatment and management of brain and spine malignancies as well as benign conditions, through innovative radiation oncology techniques. His expertise and dedication to improving patient outcomes make him a valuable addition to our team, and we are confident that his contributions will enhance the care we provide to you.

In this issue we are also excited to share a heartwarming patient success story with you. Witnessing our patients overcome challenges and achieve significant milestones is a constant reminder of why we're passionate about our work. It motivates us to continually strive for excellence in patient care and to explore cutting-edge treatment options.

At the USC Brain Tumor Center we are committed to leveraging state-of-the-art technology to enhance our diagnostic and treatment capabilities. One such technology is the **5-ALA Lighting**. This innovative approach allows neurosurgeons to visualize tumor cells with remarkable precision and accuracy. In this newsletter we delve into the benefits of this remarkable technology and how it can make a difference in the lives of many brain tumor patients.



None of this would be possible without the generosity of our dedicated donors. We are deeply grateful to all individuals and organizations who have chosen to support the USC Brain Tumor Center. Your contributions enable us to grow, advance research, invest in innovative technologies and provide compassionate care to our patients. Your generosity has profound impact in the lives of those who are affected by a brain tumor diagnosis, and we're honored to have you as part of our extended family.

As we continue to navigate the challenges posed by the treatment and cure of brain tumors, we remain steadfast in our commitment to delivering the best care possible.

We continue to grow our clinical trials portfolio, invest in cutting-edge technologies and will always provide unwavering dedication to our patients, who drive us to pursuit excellence.

Fight on!

David D. Tran, MD, PhD

Co-Director, USC Brain Tumor Center

Gabriel Zada, MD, MS, FAANS, FACS

Co-Director, USC Brain Tumor Center

Josh Neman, PhD

Scientific Director, USC Brain Tumor Center

Aram Modrek, MD, PhD Joins the USC Brain Tumor Center

The USC Brain Tumor Center and the Department of Radiation Oncology are pleased to announce our newest member of the team.

Dr. Aram Modrek, MD, PhD, is a physician-scientist who has dedicated his academic career to the study and treatment of brain tumors. He is joining the Department of Radiation Oncology and Brain Tumor Center within the USC Norris Comprehensive Cancer Center as a member of the **Genomic and Epigenomic Regulation Program**. He will have the dual role of treating patients and running a laboratory that is focused on brain tumor research. The overall mission of the collaborative laboratory is to determine how the genome is altered by DNA damage and investigate the impact of these changes on gene regulation and treatment resistance in brain tumors using cutting edge techniques and unique approaches.

He received his undergraduate degree in Biomedical Engineering from the University of California, Irvine. His career then brought him to the east coast to pursue his MD and PhD degrees at the New York University Grossman School



of Medicine through their Medical Scientist Training Program where his thesis work focused on the biology of IDH-mutated gliomas. He completed his MD/PhD training in seven years through an accelerated program that fast-tracked him into residency training in Radiation Oncology at NYU. As a resident, he was accepted into the American Board of Radiology's Holman Research Pathway - allowing him to complete post-doctoral research training with a continued focus on glioma biology, and advanced genomics and bioinformatic techniques. On a personal note, he is delighted to be returning to Los Angeles where his family resides, and to be working at an institute that he entrusts with the care of his own family.

During his academic tenure thus far, he has authored and co-authored over 20 publications on the subject of brain tumors and cancer

Continues on page 3

Glioblastoma Patient Feels Vibrant and Grateful 18-Months Post-Surgery

Della Gallagher underwent an awake craniotomy by Dr. Gabriel Zada that she recalls as a “fond memory.”

By Janice O’Leary

Gabriel Zada, MD, director of the USC Brain Tumor Center and Keck School of Medicine of USC Professor of Neurological Surgery, was recently named **Keck Medical Center of USC’s 2023 Physician of the Year**. The inaugural award was created to recognize physicians and residents who embody the enterprise’s mission, vision, and values to the fullest.

“Dr. Zada handles a large number of intricate, high-risk cases; and in those situations, the emotional needs of patients and families can be understandably high,” said Stephanie Hall, MD, chief medical officer for Keck Medical Center of USC and host of the program. “Dr. Zada advocates for his patients at every level of care.”

One of his recent high-risk patients, Della Gallagher, traveled from Canada for the benefit of his expertise. After she experienced a massive seizure in August of 2021, her doctors in Canada diagnosed her with a glioblastoma and relayed a grim prognosis.

In Alberta, Gallagher was offered surgery for a minimal reduction of the tumor. “We knew that wasn’t going to be enough,” she said. “They didn’t have the surgical skills to do more.”

As a family with deep ties to the hockey community, her husband, Ian, is an athletic coach and trainer and their son, Brendan, plays professionally for the Canadiens—a friend in the community connected her and Ian with the USC Brain Tumor Center and Dr. Zada. Within a week they had an appointment with him.

Gallagher flew to USC for Dr. Zada’s expertise, and he performed an awake craniotomy, where he removed the entire tumor and excised some of the surrounding tissue to catch any rogue cells. During the surgery, anesthesia was lifted to keep Gallagher awake for critical memory and speech monitoring, to avoid injuring any important brain pathways.

“There were 16 people in the room,” Gallagher recalls about the surgery and the team dedicated to her care. “I was talking to Rebekah [the neurosurgery nurse coordinator] the whole time and telling her some crazy stories. **Even now when I close my eyes, I can see them all. I recall that surgery with such fond memories.**”

That Gallagher’s memory is so intact is a small miracle. Often memory loss, particularly short-term memory loss, is a common side effect of

brain surgery. Her ability to describe the excellent care provided by her team of experts is even more powerful.

Following her surgery, Gallagher’s team of brain tumor experts offered her the opportunity to enroll in a **Phase III clinical trial for enzastaurin**, which has the potential to stop the growth of cancer cells. Under the care of **neuro-oncologist Frances Chow, MD and radiation oncologist Lindsay Hwang, MD**, she continues to fight her tumor with the investigational drug. “So far, I feel good, no side effects,” she said. “Being able to see the team once a month and participate in the trial gives me such hope.”



Della Gallagher (center, wearing white) with family members.

While most people would consider flying from Canada to LAX every month for more than a year and during a pandemic as a major financial and logistical obstacle, “it’s just what you do” to fight cancer said Ian.

Both Della and Ian recognize their fortune to have access to 1 of 11 brain tumor clinical trials at USC, and the highest quality of care they have received. They are particularly grateful to their son Brendan’s ability to cover costs of travel for his mother’s treatment.

Eighteen months after her first surgery, Gallagher still feels good, and her bloodwork comes back normal.

“We are stable,” said Ian. “But we’re not looking at where we’re at or where we’re going.”

“We go one day at a time,” Gallagher said. “Tomorrow it could be different. Every tumor is different.” She teared

up as she said, “Every two months I have an MRI, and we have a sleepless night. You just never know when it’s coming back.” But they have the confidence that their team at USC can fight whatever comes next.

Both Ian and Della can’t say enough about the quality of care and attention they’ve received from the entire staff, from the one-to-one nurse who styled her hair every day post-surgery to the staff who helped with the mountains of insurance paperwork and the physicians who keep searching for a cure.

At home in Canada, they’d have to wait so long just to schedule an MRI. Here with their USC family, access to MRIs can be scheduled within hours and “the care is awesome.”

“Aram Modrek MD, PhD...” continued

biology and has given oral presentations on his research at national and international conferences including American Association for Cancer Research (AACR), Society for Neuro-Oncology (SNO) and World Federation of Neuro-Oncology Society (WFNOS). He has received numerous research awards and recognitions including the AACR/ABTA travel-grant and the RSNA Roentgen Resident Research Award. His research has been supported by grant funding through the American Brain Tumor Association, Radiological Society of North America, Novocure, and has ongoing funding through a five-year National Institutes of Health (NIH)/National Cancer Institute (NCI) Career Development Award.

Dr. Modrek served as a Chief resident in his residency and had a training experience that was enriched for neuro-radiation oncology. This has allowed him to bring together his career passions on two fronts: patient-forward care and cutting-edge research. His training in a multi-disciplinary environment focused on patient-centered care to provide the best possible outcomes.

He brings with him experience in the treatment and management of brain and spine malignancies, and benign conditions, through advanced radiation oncology techniques. These techniques include intensity-modulated radiation therapy (IMRT) with image guidance, stereotactic body radiotherapy for spine and brain tumors, re-irradiation, Novocure optune treatment (tumor treating fields), and gamma-knife based radiosurgery for brain tumors and benign conditions. Importantly, he believes our most important technique isn't necessarily a machine or tool, but simply sharing our compassion and earning our patient's trust through their challenging journey.

Gabriel Zada, MD, Director of the USC Brain Tumor Center, is named Physician of the Year

In a ceremony on the Health Sciences Campus on May 31, Gabriel Zada, MD, Director of the USC Brain Tumor Center, was named **Keck Medical Center of USC's Physician of the Year**. This was the organization's inaugural Physician of the Year event and was meant to recognize physicians and residents who embody the enterprise's mission, vision, and values to the fullest.

“Dr. Zada handles a large number of intricate, high-risk cases; and in those situations, the emotional needs of patients and families can be understandably high,” said Stephanie Hall, MD, chief medical officer for Keck Medical Center of USC and host of the program. “Dr. Zada advocates for his patients at every level of care and treats every team member with respect.”

Dr. Zada is a board-certified neurosurgeon and internationally recognized expert in brain, skull base and pituitary tumor surgery, as well as a variety of endoscopic and minimally invasive neurosurgical techniques. He has treated over 2,000 patients with brain and skull base tumors using both minimally invasive and open cranial approaches.

Keck Medical Center of USC's Physician and Resident of the Month program launched in August of 2021. Each month, a physician and resident who practice at



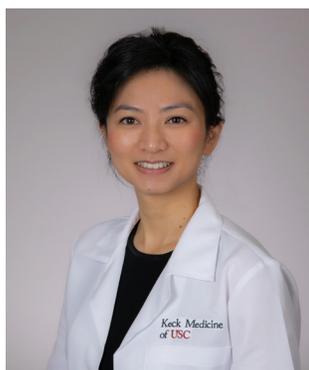
the medical center or a USC Care facility are selected based on submissions received from employees across the organization. The goal of the program is to select physicians and residents who best represent the organization's 5-star principles, and who uphold behaviors that create the best experience for everyone receiving care at the enterprise.

For the 2023 Physician and Resident of the Year program, nominees consisted of each month's winners from the 2022 calendar year. A committee made up of medical staff and administrative leaders then made final selections for the 2023 award winners.

USC Brain Tumor Center Announcements

We are excited to welcome the newest **Norris Disease Affinity Group (DAG)**. The **Neuro-Oncology DAG** will bring together clinicians, basic scientists, and population scientists who treat and study primary neurologic malignancies and CNS metastasis.

As with all DAGs, the goal will be to catalyze multi-disciplinary translational collaborations leading to new papers, grants, and trials.



Frances Chow, MD

The new DAG will be co-led by **Dr. Frances Chow**, Assistant Professor of Clinical Neurological Surgery & Neurology and by **Dr. Josh Neman**, Assistant Professor of Neurological Surgery, Physiology & Neuroscience. Drs. Chow and Neman bring an exceptional breadth of expertise spanning basic, translational, and clinical neuro-oncology, and they already play key roles in USC's Brain Tumor Center. As such, they exemplify multi-disciplinary collaboration in this field.

In addition, we are pleased to announce the appointment of **Dr. Josh Neman** as the new **Associate Director for Cancer Research Training and Education Coordination (CRTEC)** at the USC Norris Comprehensive Cancer Center effective July 1, 2023.

Dr. Neman will create and oversee cancer research education and training initiatives across the continuum from pre-collegiate to faculty training.

Supported by the **National Cancer Institute**, CRTEC's mission is to prepare the next generation of basic, translational, clinical, and population scientists, with a focus on convergent minds, inclusion, and diversity.



Josh Neman, PhD

USC Brain Tumor Center Development

In the third year since relaunching the USC Brain Tumor Center, we are grateful to our loyal community of donors and are inspired by their commitment to supporting the cutting-edge clinical, research, and educational efforts of the USC BTC.

This fiscal year (July 1, 2022 to June 30, 2023), the USC BTC reached a new peak in its fundraising totals-- raising over \$270,000 in gifts from 223 donors. These gifts provided critical resources to maintain the state-of-the-art equipment and technology used in the research labs, as well as helping to launch clinical trials and other efforts that will lead to further discoveries and better patient care.

We want to thank everyone for their generosity and give mention to a few of our standout partners. This year, the **Brain Tumor Companion** patient community group selected the research efforts of the USC Brain Tumor Center as recipient of their annual fundraising campaign. Thus far, their efforts have amounted to nearly \$17,000—with several more months to reach their goal of \$50,000.

Additionally, the USC Brain Tumor Center is appreciative to the **Smith Brothers Restaurants (Parkway Grill, Arroyo Chop House, Smitty's)**

and their commitment to supporting the USC BTC with a portion of Thursday sales through the months of May, June, and July.

Finally, we extend our sincere gratitude to **Dr. Robert Kolesnik** for his generous gift of \$50,000 this spring. Dr. Kolesnik is a super Trojan, completing his Bachelors, MD and Residency at USC. With his generosity expanding across multiple areas of campus, the USC BTC is proud to be a part of his inspiring legacy.

Also, a big thank you to the **USC Brain Tumor Center Advisory Council**, who provide insight on strategy to increase the USC BTC's profile, both clinically and as a philanthropic opportunity. The members of our USC Brain Tumor Center Advisory Council include: **David J. Aroesty; Julieta Bennett; Alexandra Clark; Andre Hudy; Esther Kim; Karen Landry; Thomas Palffy; Kelly and Joe Self; Anna Zaich.**

A thank you to all as we look forward to continuing this upward trajectory to propel the USC BTC mission forward. If you would like to explore how you can make an impact, or discuss joining our Advisory Council, please feel free to contact **Nicole Measles, Director of Development**, at **Nicole.Measles@med.usc.edu** or **213-806-0693**.



1st Annual Southern California BRAIN TUMOR CONFERENCE

Hosted by Keck Medicine of **USC**

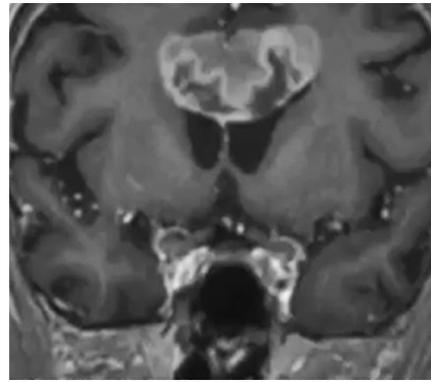
Friday, December 8, 2023 • 8:00am - 4:30pm



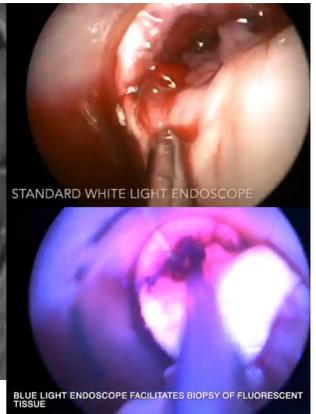
Fluorescent Tumor Cells Improve Surgical Resection

Complete (gross total) resection of brain tumors is critical to achieving extended patient survival. However, gross total resection is often extremely challenging, as tumors (particularly gliomas) appear indistinguishable from normal, surrounding brain tissue. At the USC Brain Tumor Center, we utilize the novel tumor-visualization compound, **5-aminolevulinic acid (5-ALA)**. Tumor cells that absorb 5-ALA emit bright fluorescent

light when under our operative microscopes, allowing our neurosurgeons to visualize tumor cells with remarkable precision and accuracy. The surgeon leverages the pink light by tumor cells to focus resection on fluorescent tissue while keeping healthy (and non-fluorescent) brain unharmed. Studies from USC and other institutions have shown significantly improved rates of gross total resection and patient survival when utilizing 5-ALA with surgical resection.



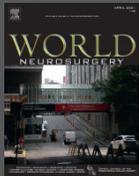
RIGHT FRONTAL BIOPSY of GBM via 11MM CHANNEL APPROACH



STANDARD WHITE LIGHT ENDOSCOPE

BLUE LIGHT ENDOSCOPE FACILITATES BIOPSY OF FLUORESCENT TISSUE

SELECTED PUBLICATIONS

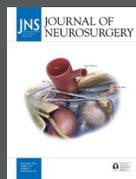


5-ALA Enhanced Fluorescence-Guided Microscopic to Endoscopic Resection of Deep Frontal Subcortical Glioblastoma Multiforme. Strickland BA, Zada G.

World Neurosurg. 2021 Apr;148:65. doi: 10.1016/j.wneu.2020.12.168. Epub 2021 Jan 13. PMID: 33453427.

■ Glioblastoma multiforme remains the most common adult primary brain tumor with a life expectancy of 15-18 months following best treatment strategies. Current paradigms incorporate maximal safe resection, chemotherapy, and radiation.¹ Multiple variables correlate with increased survival; perhaps most notably are step-wise survival advantages following 78% and 98% extent of resection thresholds.^{2,3} 5-Aminolevulinic acid has become a vital tool in the intraoperative identification and differentiation of high-grade glioma as it provides a fluorescent effect capable of distinguishing tumor from normal brain tissue when observed under blue light, which to date has been used primarily via a microscopic light source.⁴ However, this effect is attenuated with increasing distance between the blue light source and the tumor, as in the case of deep seated resection cavities.⁵ We aimed to overcome this obstacle by using a blue light endoscope as the primary visualization platform, thereby advancing the light source directly into the resection cavity. We present the case of a 69-year-old man with a deep left frontal subcortical lesion proven to be glioblastoma multiforme on prior biopsy. He consented to undergo an inter-hemispheric "M2E" (microscopic-to-endoscopic) approach with subcortical motor mapping. Tumor fluorescence under blue light visualization was not appreciated by

the operating microscope but was easily observed with the blue light endoscope. Tumor resection proceeded under direct blue light endoscopy with intermittent subcortical motor mapping until a threshold of 4 mA was reached. The patient had transient right arm and leg weakness. Postoperative magnetic resonance imaging confirmed >98% resection.



5-Aminolevulinic acid-enhanced fluorescence-guided treatment of high-grade glioma using angled endoscopic blue light visualization: technical case series

with preliminary follow-up. Strickland BA, Wedemeyer M, Ruzevick J, Micko A, Shahrestani S, Daneshmand S, Shiroishi MS, Hwang DH, Attenello F, Chen T, Zada G. *J Neurosurg.* 2022 Mar 18:1-9. doi:10.3171/2022.1.JNS212562. PMID: 35303704.

■ **Objective:** 5-Aminolevulinic acid (5-ALA)-enhanced fluorescence-guided resection of high-grade glioma (HGG) using microscopic blue light visualization offers the ability to improve extent of resection (EOR); however, few descriptions of HGG resection performed using endoscopic blue light visualization are currently available. In this report, the authors sought to describe their surgical experience and patient outcomes of 5-ALA-enhanced fluorescence-guided resection of HGG using primary or adjunctive endoscopic blue light visualization.

■ **Methods:** The authors performed a retrospective review of prospectively collected data from 30 consecutive patients who underwent 5-ALA-enhanced fluorescence-guided biopsy or resection of newly diagnosed HGG was performed. Patient

demographic data, tumor characteristics, surgical technique, EOR, tumor fluorescence patterns, and progression-free survival were recorded.

■ **Results:** In total, 30 newly diagnosed HGG patients were included for analysis. The endoscope was utilized for direct 5-ALA-guided port-based biopsy (n = 9), microscopic to endoscopic (M2E; n = 18) resection, or exoscopic to endoscopic (E2E; n = 3) resection. All endoscopic biopsies of fluorescent tissue were diagnostic. 5-ALA-enhanced tumor fluorescence was visible in all glioblastoma cases, but only in 50% of anaplastic astrocytoma cases and no anaplastic oligodendroglioma cases. Gross-total resection (GTR) was achieved in 10 patients in whom complete resection was considered safe, with 11 patients undergoing subtotal resection. In all cases, endoscopic fluorescence was more avid than microscopic fluorescence. The endoscope offered the ability to diagnose and resect additional tumor not visualized by the microscope in 83.3% (n = 10/12) of glioblastoma cases, driven by angled lenses and increased fluorescence facilitated by light source delivery within the cavity. Mean volumetric EOR was 90.7% in all resection patients and 98.8% in patients undergoing planned GTR. No complications were attributable to 5-ALA or blue light endoscopy.

■ **Conclusions:** The blue light endoscope is a viable primary or adjunctive visualization platform for optimization of 5-ALA-enhanced HGG fluorescence. Implementation of the blue light endoscope to guide resection of HGG glioma is feasible and ergonomically favorable, with a potential advantage of enabling increased detection of tumor fluorescence in deep surgical cavities compared to the microscope.

**CLINICAL TRIALS:
Now Enrolling at the USC Brain
Tumor Center**

Have you or someone you know recently been diagnosed with a brain tumor? Choosing the right treatment can be challenging. To find out more about our breakthrough treatments, contact our specialized brain tumor team at **(844) 33-BRAIN (844-332-7246)** or email frances.chow@med.usc.edu.

A Phase 1/2 Trial of Selinexor and Temozolomide in Recurrent Glioblastoma

Selinexor is a novel first-in-class XPO1 inhibitor with potent anti-tumor activity. Preclinical studies demonstrate that selinexor blocks nuclear export, impairs DNA repair, and triggers tumor cell death. Through the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program, Dr. Frances Chow led a team of cancer biologists, pharmacists, and translational scientists to develop a clinical trial to evaluate the safety and efficacy of temozolomide in combination with selinexor in recurrent glioblastoma.

This study is supported by the National Institutes of Health (NIH) and is currently enrolling at USC and across the Experimental Therapeutics Clinical Trials Network (ETCTN).

Trial	Interventions	Phase
Brain Metastasis		
1 Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy	<ul style="list-style-type: none"> • GammaTile • Stereotactic radiosurgery 	Phase 1
Glioblastoma		
2 A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	<ul style="list-style-type: none"> • Selinexor + Temozolomide • Temozolomide 	Phase 1/2
3 An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma	<ul style="list-style-type: none"> • Perillyl alcohol (inhaled) 	Phase 1/2A
4 A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants With Previously Treated Glioblastoma or Other Primary Central Nervous System Tumors Harboring Activating FGFR 1-3 Alterations (FIGHT-209).	<ul style="list-style-type: none"> • Pemigatinib 	Phase 2
5 Testing the Addition of the Immune Therapy Drugs, Tocilizumab and Atezolizumab, to Radiation Therapy for Recurrent Glioblastoma (BN010)	<ul style="list-style-type: none"> • Radiation + Tocilizumab + Atezolizumab • Radiation + Tocilizumab 	Phase 2
6 Enzastaurin Plus Temozolomide During and Following Radiation Therapy in Patients with Newly Diagnosed Glioblastoma with or Without the Novel Genomic Biomarker, DGM1	<ul style="list-style-type: none"> • Enzastaurin + Standard therapy • Standard therapy 	Phase 3
7 GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	<ul style="list-style-type: none"> • GammaTile + Standard therapy • Standard therapy 	Phase 4
8 Pivotal, Randomized, Open-label Study of Optune® Concomitant with RT & TMZ for the Treatment of Newly Diagnosed GBM (EF-32)	<ul style="list-style-type: none"> • Optune + Standard therapy • Standard therapy 	N/A
Meningioma		
9 An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	<ul style="list-style-type: none"> • Perillyl alcohol (inhaled) 	Phase 2
10 Observation or Radiation Therapy in Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)	<ul style="list-style-type: none"> • Radiation • Standard therapy 	Phase 3

USC Brain Tumor Center

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Patient referrals, (844) 33-BRAIN (844-332-7246)

At the USC Brain Tumor Center, our mission is to provide exceptional, comprehensive and innovative concierge-style treatment plans for adults and children with all types of brain tumors and related conditions. Giveto.USC.edu

We Are the USC Brain Tumor Center

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USC Brain Tumor Center



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To refer a patient, please call **(844) 33-BRAIN (844-332-7246)**

Make a Gift. Because of your support, we can provide Exceptional Medicine. Please contact **Brian Loew**, Senior Director of Development, Neurosciences, at Brian.Loew@med.usc.edu or visit www.keckmedicine.org/btc-donations

For more information about brain tumor clinical trials, please contact **Aida Lozada**, Clinical Trials Manager, at Aida.Lozada@med.usc.edu

Please email us with your questions at BTC@med.usc.edu



Learn more at: BTC.keckmedicine.org