The Official Newsletter of the
Keck Medicine of USC
USC Brain Tumor Center
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USC Norris Comprehensive Cancer Center
Keck Medicine of USC

USC BRAIN TUMOR CENTER Report

Volume 4 ▪ Issue 4
AUTUMN 2024

From the USC BTC Directors

The year 2024 has been exceptional for the USC Brain Tumor Center! We are thrilled to begin this quarterly newsletter by celebrating the remarkable achievements of our multidisciplinary team. Several of our members have earned prestigious awards and secured grants that will propel our research efforts toward finding a cure for brain tumors. We extend heartfelt congratulations to everyone involved.

Our inspiration comes from our patients, who drive us to push the boundaries of brain tumor care and treatment. In this edition, we feature an insightful piece on the importance of palliative care from the perspective of our dedicated social worker, **Jinsy Rogers**.

This year, we were honored to be gold sponsors of the **American Brain Tumor Association (ABTA) Annual Conference**, held in Chicago in September. We also joined the **ABTA BT5K annual walk** in Santa Monica in October, reaffirming our commitment to supporting the broader brain tumor community in any way we can.

Raising awareness is crucial in order to secure more funding and develop research aimed at curing brain cancer. This fall, the Brain Tumor Center hosted an engaging lecture series on brain health at a club in Pasadena, demonstrating our commitment to community education.

Collaboration is key when tackling brain tumors. This year, we co-hosted the **25th Annual Brain Tumor Update** and **14th Annual Symposium on Brain Metastases and Spine Tumors** held in Los Angeles in collaboration with the Cleveland Clinic.

Looking ahead, we are excited to welcome experts from eight Southern California institutions for the **2nd Annual Brain Tumor Conference** on December 6, 2024. This event will focus on addressing challenges and fostering collaboration among scientific and healthcare professionals committed to brain tumor research and treatment.

The USC Brain Tumor Center continues to expand its extensive clinical trial portfolio, with several new trials for glioblastoma, brain metastases, and meningiomas launching soon.

We sincerely thank you for supporting our mission to provide unparalleled clinical care and to work tirelessly toward curing brain tumors.

Heal 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

Message from the Chair of Neurosurgery

William J. Mack, MD, MBA, Professor and Chair, Department of Neurological Surgery

As Chair of the Keck Medicine of USC Department of Neurosurgery, I want to reaffirm my unwavering support for the USC Brain Tumor Center, a cornerstone of our department's commitment to advancing patient care, education, and research. The work being done here is truly transformative—enhancing patient outcomes, pioneering groundbreaking research, and providing hope to countless individuals and families navigating complex brain tumor diagnoses.

Our faculty, staff, and researchers within the USC Brain Tumor Center are among the best, consistently demonstrating the highest levels of skill, innovation, and compassion.

I am proud of their efforts, from performing cutting-edge surgeries to developing new treatment protocols, and I am committed to ensuring they have the resources and support needed to continue their exceptional work.

I encourage each of you to engage actively with the Center's initiatives, whether through collaborative research, clinical care, educational endeavors, or outreach programs.

Together, we can drive the kind of progress that can change lives.

Thank you for your dedication, and let's continue to make strides in our mission to improve the lives of patients facing brain tumors.

Congratulations to USC Brain Tumor Center Grant Recipients


Gabriel Zada, MD, MS

I am thrilled to extend my heartfelt congratulations to several esteemed members of our multidisciplinary team for the prestigious awards and grants they have received this year.

Your unwavering dedication and innovative work in advancing brain tumor research are truly admirable. These accomplishments not only recognize your hard work but also empower us to make even greater strides toward finding a cure.

Thank you for your continued commitment and excellence.

Frances Chow, MD

Dr. Frances Chow was awarded the **Robert A. Winn Diversity in Clinical Trials: Career Development Award**. The Winn CDA award is a 2-year career development program providing $240,000 for physicians who have demonstrated commitment to increasing diversity in clinical research.

The program's goal is to support the development of independent clinical trial investigators who are engaged in advancing health equity. Dr. Chow's project will enhance relationships with the Los Angeles community by improving access to clinical trials and specialized brain tumor care.

The Winn CDA is supported by the Bristol Myers Squibb Foundation and training is conducted in partnership with the American Association of Cancer Research (AACR).

In addition to the Winn CDA award, **Dr. Frances Chow** was awarded the **Norris Liquid Biopsy Grant**. The current approaches to glioblastoma diagnosis and response to therapy involve surgery and imaging. However, both techniques have inherent limitations.


Frances Chow, MD

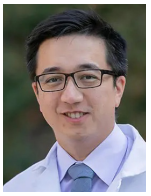
Surgery can pose challenges in certain locations of the brain and imaging can be inconclusive when discerning between pseudoprogression versus true progression of disease.

Thus, liquid biopsy has emerged as a promising, less-invasive diagnostic tool to address the unmet need of early diagnosis and detection of tumor recurrence.

Dr. Chow's project is a pilot study to develop a workflow to identify glioma stem cells in patient blood and CSF.

Frank Attenello, MD, MS

Dr. Frank Attenello received $100,000 **Wright Foundation Transformative Research Grant**. The Wright Foundation supports projects that generate preliminary data in support of innovative and high impact research related to arthritis, cancer, or heart disease.


Frank Attenello, MD, MS

This grant will fund his study identifying the mechanism by which microenvironment regulates dormant glioma stem cells.

"Treatment resistance is one of the largest barriers to patient improvement. Our lab has identified specific metabolism alterations regulating a subset of treatment resistant cells. Notably, this resistant cell population is capable of changing its identity in response to multiple environmental factors.

Our study, generously funded by the Wright Foundation, will allow us to further explore microenvironmental factors that control this cell population and its response to treatment."

Aram Modrek, MD, PhD


Aram Modrek, MD, PhD

The Modrek Laboratory received new funding from several sources this year. This included the **Baxter Foundation Grant**, **V Foundation Grant**, the **American Cancer Society Institutional Research Grant**, and the **USC Norris Epigenetic Regulation in Cancer Program Pilot Award**. The Modrek laboratory continues to also receive funding through the National Institutes of Health (NIH) via the National Cancer Institute.

This support from the NIH and foundation grants was possible thanks to the support of the Brain Tumor Center, collaborative environment, and senior mentorship from **Dr. Eric Chang**, **Dr. David Tran**, and **Dr. Yali Dou**.

With this new funding the Modrek laboratory will continue to grow and pursue high-risk-high reward projects such as single-cell studies of how glioblastoma evolves during treatment, explore how the DNA of tumor cells are chemically modified during therapy using single-molecule techniques, and conduct high-throughput screens of genes that may be involved in treatment resistance.

Khoi Huynh, PhD


Khoi Huynh, PhD

Dr. Khoi Huynh received the **Margaret Kersten Ponty Endowed Postdoctoral Fellowship Award in Oncology Research** at the Norris Comprehensive Cancer Center. This endowed postdoctoral fellowship comes with a $50,000 award.

Dr. Huynh is a post-doctoral scholar in the Modrek lab within the Department of Radiation Oncology, he is also co-mentored by **Dr. David Tran** from the Department of Neurosurgery.

His research focus is on glioblastoma and response to radiation therapy.

Palliative Care for a Brain Tumor Diagnosis

By Jinsy Rogers, LCSW, OSW-C


Jinsy Rogers, LCSW

Recently, when I spoke to a patient about the benefits of having Palliative Care on board as part of their medical team, I registered a look of fear of their face. My patient explained that every time he had heard the word Palliative Care, he immediately thought "end of life care". It worried him even more as he was just beginning his chemotherapy and radiation treatments. It's a very common misconception that Palliative Care = Hospice.

Palliative Care is a wonderful resource as it offers a team that looks at the patient as a whole, considering their quality of life as they undergo cancer treatment. Palliative care can help to manage uncomfortable symptoms while patients are undergoing chemo/radiation therapies.

They can work alongside your oncology team to assure that not only symptoms are being addressed but that cancer directed therapies are aligned with a patient's values and goals. After meeting with our Palliative Care physician, my patient felt a sense of relief in knowing that he had a team to address uncomfortable symptoms that may arise throughout his treatment and to help him to achieve the best quality of life he could have.

If you would like to explore how Palliative Care can be beneficial for you, speak with your Oncology team for a referral.

The USC Brain Tumor Center is a Gold Sponsor of the 2024 American Brain Tumor Association National Conference

The USC Brain Tumor Center was a sponsor of the 2024 American Brain Tumor Association National Conference in September, joined by other healthcare institutions, pharmaceutical and medical device companies, as well as non-profit foundations.

Attendance for patients and caregivers was offered both in-person and virtually, with record setting in-person attendance!

The two-day meeting included general sessions, including a Tumor Board run through, and many of options of small group sessions covering exercise and nutrition to a physician led discussion on "What if My Tumor Comes Back?"

Break time with snacks provided opportunity for patients to meet and share their own journey with one another.

It was so great to see patients networking, and perhaps forgetting they were patients for a moment, just learners for a few days.

"This conference gave me confidence and reminded me that I am not alone in this and there are whole teams of doctors, researchers, nurses and advocates that are diligently and passionately working on solving this problem. That was incredible to see all under one roof!"

We look forward to supporting the ABTA and representing the BTC in 2025!

Left to right: Jinsy Rogers, LCSW, Nancy Hart, RN, MSN, CPON, and Ralph DeVitto, President and CEO, ABTA

The USC Brain Tumor Center shows up in great form to Raise Funds at the ABTA BT5K

A beautiful Saturday morning in Santa Monica on October 26th was the setting for the USC Brain Tumor Center Team and their families as they came together to run/walk the American Brain Tumor Association BT5K.

The USC Brain Tumor Center was a Silver Sponsor for the **American Brain Tumor Association Annual Breakthrough for Brain Tumors BT5K- Los Angeles**. **Dr. Gabriel Zada**, Co- Director of the USC BTC, **Dr. Aram Modrek**, radiation oncologist for the USC BTC & the USC Norris Comprehensive Cancer Center and **Paola Mork**, Manager of the USC BTC were part of the Host Committee. **Dr. Josh Neman**, Scientific Director of the USC BTC, spoke as part of a panel about the future of brain tumor research. The funds raised by this event support the ABTA's mission of providing critical funding for brain tumor research and patient support services. Thank you to all who joined our team!

We look forward to sponsoring the ABTA again next year and we hope that you can join us in supporting this wonderful organization.

The USC Brain Tumor Center Hosts an Evening of Presentations at a Private Club in Pasadena

On September 24th, 2024, the USC Brain Tumor Center had the honor of hosting an informational dinner at a prestigious private club in Pasadena.

Insights into Prevention and Management of Brain Disease in 2024: a Conversation about Alzheimer's, Dementia, Stroke and Brain Tumor Center with Keck Medicine of USC Physicians, is a talk series presented by Keck Medicine of USC Faculty to the community.

Dr. Steven Giannotta, Professor and esteemed Past Chair of USC's Neurosurgery department, presented speakers, **Dr. Arun Amar** (Neurosurgery), **Dr. Hussein Yassine** (Neurology), and **Dr. Gabriel Zada** (Brain Tumor Center). It was a resounding success and a significant event for USC's Neurosurgery and Neurology departments. The dinner not only served as a platform to share state-of-the-art treatments and research but also strengthened the connection between USC's medical advancements and the community. It's clear that the event was both informative and well-received, setting the stage for continuing engagements aimed at further educating and engaging the public.

For updates on future events hosted by the Brain Tumor Center and USC's Neuroscience department, interested individuals are encouraged to follow them on Instagram.

USC Brain Tumor Center Hosts Second Annual Brain Tumor Conference

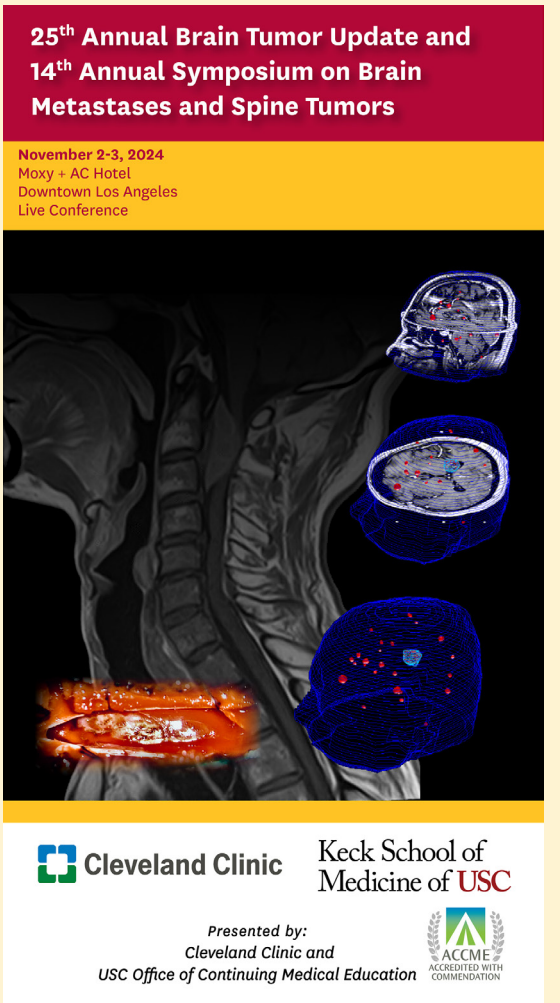
To advance brain tumor research, treatment, and therapies, the USC Brain Tumor Center will again organize and host the **2nd Annual Southern California Brain Tumor Conference** which will be held in person at the USC Health Sciences Campus on December 6, 2024.

To address the challenges and foster collaboration among scientific and healthcare professionals focusing on brain tumors in Southern California, the conference brings together 8 perennial academic and hospital institutions together -- **USC**, **CHLA**, **UCLA**, **UCI**, **UCSD**, **City of Hope**, **Cedars Sinai**, and **Pacific Neuroscience Institute**.

The 2nd annual Southern California Brain Tumor Conference provides a platform for researchers and clinicians to share and discuss the latest discoveries, fostering scientific exchange, and promoting the translation of research into clinical practice. Brain tumor teams from these perennial institutions—from trainees, to administrators, researchers, clinicians, and faculty — along with members of the community-at large came together this year, to share our visions for the future of brain tumor research and care.

This year the conference's format will be divided into five sessions: **Session 1: High-Grade Gliomas**, **Session 2: Brain Metastases**, **Session 3: Meningioma/Pituitary**, **Session 4: Pediatric Brain Tumors**, and **Session 5: Palliative Care**. We will also have a poster session at the end of the conference.

We look forward to welcoming researchers, clinicians, patients, and caregivers from Southern California and are having the option of joining in a hybrid manner for those who prefer to participate remotely.



The 25th Annual Brain Tumor Update and the 14th Annual Symposium on Brain Metastases and Spine Tumors co-hosted by the Keck School of Medicine of USC and Cleveland Clinic

Keck Medicine of USC and Cleveland Clinic co-hosted the **25th Annual Brain Tumor Update and 14th Annual Symposium on Brain Metastases and Spine Tumors** at the Moxy + AC Hotel in DTLA on November 2-3, 2024 as a live conference.

This advanced multidisciplinary meeting was led by expert faculty from Cleveland Clinic and USC, with additional internationally recognized guest faculty.

As neurological complications and extending survival from primary and secondary tumors of the brain and spine continue to be a challenge, a wide variety of talks were given on gliomas, spine tumors, and brain metastases. There was also a session dedicated to pituitary tumors.

CONFERENCE AGENDA

Session I: High-Grade Gliomas

- **Modeling Genetic Heterogeneity of Glioblastoma and Response to Standard of Care Treatment in the Immunocompetent Mouse:** Katie Grausam, PhD
- **Clinical Trial Through ETCTN for Patients with Recurrent High-Grade Glioma:** Stephanie Yoon, MD
- **Updates in Resection of Gliomas:** Aaron Cohen-Gadol, MD
- **Neo 100:** Thomas C. Chen, MD, PhD
- **In Situ Vaccination of Brain Tumors:** David D. Tran, MD, PhD
- **UHuman iPSC-Derived Brain Cancer Avatars: Lessons Learned and Opportunities for Therapeutic Recovery:** Frank Furnari, MD

Session II: Brain Metastases

- **Functional Magnetic Resonance Imaging (fMRI) as Adjunct for Planning Laser Interstitial Thermal Therapy (LITT) Near Eloquent Structures:** Won Kim, MD
- **Cancer Neuroscience in Brain Metastasis:** Josh Neman, PhD
- **Chimeric Antigen Receptor (CAR) T Cell Therapy for Leptomeningeal Disease from Primary Brain Tumors:** Lisa Anne Feldman, MD, PhD

Session III: Meningioma/Pituitary

- **Advances in Minimally Invasive Cranial Neurosurgery in 2025:** Gabriel Zada, MD, MS
- **Radiosurgery for Benign Brain Tumors:** Jason C. Ye, MD
- **Mechanisms of Radiation Resistance:** Aram Modrek, MD, PhD
- **Endocrine Outcomes After PItuitary Tumor Surgery:** Garni Barkhoudarian, MD

Session IV: Pediatric Brain Tumors

- **G34R Gliomas :** David Rincón Fernandez Pacheco, PhD
- **Immunometabolic Adaptation of CD19-Targeted CAR T Cells in the CNS Microenvironment of Patients Promotes Memory Development:** Lior Goldberg, MD, MS
- **Liquid Biopsy Platform :** Katrina O'Halloran, MD, MS
- **Mechanism(s) of Brain Tumor Growth Inhibition by PID1 :** Anat Erdreich-Epstein, MD, PhD
- **Animal Modeling of Recurrent Somatic Mutations-Towards Personalized Models of Pediatric Brain Tumors :** Moise Danielpour, MD

Session V: Palliative Care

- **Whole Person Care- How Palliative Care Integration Improves the Care of Neuro Oncology Patients:** Akanksha Sharma, MD

Friday, December 6, 2024 • 7:30 am - 5:30 pm

HSC Conference Center on the **USC Health Sciences Campus**
2200 Trojan Way, Los Angeles, CA 90033
Entrance on San Pablo St., North of Alcazar St.

Learn more about the **Southern California Brain Tumor Conference** at:
https://keckusc.cloud-cme.com/course/course-overview?P=0&EID=7952

Cedars Sinai | Children's Hospital Los Angeles | City of Hope | Keck Medicine of USC | Pacific Neuroscience Institute | UC Irvine Health School of Medicine | UCLA David Geffen School of Medicine | UC San Diego School of Medicine

Hayden M. Gidan Compassionate Care Fund to Support Palliative Care Presentation at the Annual Southern California Brain Tumor Conference

Nicole Measles

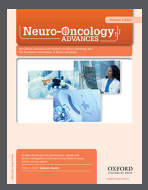
We imagine a world where a brain tumor diagnosis comes with far less fear and much more hope. Every day our team at the USC Brain Tumor Center is working towards making that a reality through compassionate clinical care with a comprehensive team approach, and through research efforts led by our experts in multiple brain tumor research laboratories.

We are so grateful for the partnership of our generous donors and for the initiatives they sponsor. For a 2nd year, we are excited to highlight the importance of compassionate care at our **Annual Southern California Brain Tumor Conference**.

Supported by the Gidan family through the **Hayden M. Gidan Compassionate Care Fund**, this year's speaker is **Dr. Akanksha Sharma** who will give a talk entitled, ***"Whole Person Care – How Palliative Care Integration Improves the Care of Neuro Oncology Patients"***. We know Dr. Sharma will make a lasting impression on this year's attendees, and are grateful for the lessons that attendees will be able to take back to their respective institutions and patients.

If you would like to support our Center in a way most meaningful to you, please feel welcome to email **Nicole Measles**, Director of Development, Neurosciences at **Nicole.measles@med.usc.edu** or call **(213) 806-0693**.

SELECTED PUBLICATIONS

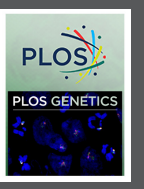


Modulating glioblastoma chemotherapy response: Evaluating long non-coding RNA effects on DNA damage response, glioma stem cell function, and hypoxic processes. ***Yuan E, Liu K, Lee J, Tsung K, Chow F, Attenello FJ.*** *Neurooncol Adv. 2022 Aug 10;4(1):vdac119. doi: 10.1093/noajnl/vdac119. PMID: 36105389; PMCID: PMC9466271.*

Glioblastoma (GBM) is the most common and aggressive primary adult brain tumor, with an estimated annual incidence of 17 000 new cases in the United States. Current treatments for GBM include chemotherapy, surgical resection, radiation therapy, and antiangiogenic therapy.

However, despite the various therapeutic options, the 5-year survival rate remains at a dismal 5%. Temozolomide (TMZ) is the first-line chemotherapy drug for GBM; however, poor TMZ response is one of the main contributors to the dismal prognosis. Long non-coding RNAs (lncRNAs) are nonprotein coding transcripts greater than 200 nucleotides that have been implicated to mediate various GBM pathologies, including chemoresistance.

In this review, we aim to frame the TMZ response in GBM via exploration of the lncRNAs mediating three major mechanisms of TMZ resistance: (1) regulation of the DNA damage response, (2) maintenance of glioma stem cell identity, and (3) exploitation of hypoxia-associated responses.



CRISPRi screen of long non-coding RNAs identifies LINC03045 regulating glioblastoma invasion. ***Tsung K, Liu KQ, Han JS, Deshpande K, Doan T, Loh YE, Ding L, Yang W, Neman J, Dou Y, Attenello FJ.*** *PLoS Genet. 2024 Jun 10;20(6):e1011314. doi: 10.1371/journal.pgen.1011314. PMID: 38857306; PMCID: PMC11192328.*

Introduction: Glioblastoma (GBM) invasion studies have focused on coding genes, while few studies evaluate long non-coding RNAs (lncRNAs), transcripts without protein-coding potential, for role in GBM invasion.

We leveraged CRISPR-interference (CRISPRi) to evaluate invasive function of GBM-associated lncRNAs in an unbiased functional screen, characterizing and exploring the mechanism of identified candidates.

Methods: We implemented a CRISPRi lncRNA loss-of-function screen evaluating association of lncRNA knockdown (KD) with invasion capacity in Matrigel. Top screen candidates were validated using CRISPRi and oligonucleotide (ASO)-mediated knockdown in three tumor lines. Clinical relevance of candidates was assessed via The Cancer Genome Atlas (TCGA) and Genotype-Tissue Expression (GTEx) survival analysis. Mediators of lncRNA effect were identified via differential expression analysis following lncRNA KD and assessed for tumor invasion using knockdown and rescue experiments.

Results: Forty-eight lncRNAs were significantly associated with 33-83% decrease in invasion ($p<0.01$) upon knockdown. The top candidate, LINC03045, identified from effect size and p-value, demonstrated 82.7% decrease in tumor cell invasion upon knockdown, while LINC03045 expression was significantly associated with patient survival and tumor grade ($p<0.0001$). RNAseq analysis of LINC03045 knockdown revealed that WASF3, previously implicated in tumor invasion studies, was highly correlated with lncRNA expression, while WASF3 KD was associated with significant decrease in invasion. Finally, WASF3 overexpression demonstrated rescue of invasive function lost with LINC03045 KD.

Conclusion: CRISPRi screening identified LINC03045, a previously unannotated lncRNA, as critical to GBM invasion.

Gene expression is significantly associated with tumor grade and survival. RNA-seq and mechanistic studies suggest that this novel lncRNA may regulate invasion via WASF3.

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.

TVAX BIOMEDICAL®

Newly Open: USC partners with TVax Biomedical to open the TVI-Brain-1 cancer vaccine

The USC Brain Tumor Center is now recruiting patients to a phase 2b personalized vaccine-based immunotherapy trial for newly diagnosed glioblastoma. TVI-Brain-1 (TVax Biomedical) is a treatment that uses each patient's own cancer cells collected during surgery to create a cancer-targeting vaccine. When the body is exposed to the vaccine, it stimulates T cells, which are harvested from the blood and are subsequently stimulated, expanded, and infused back to the patient. ClinicalTrials.gov identifier NCT05685004.

	Trial	Interventions	Phase
	Brain Metastasis		
1	Stereotactic Radiosurgery (SRS) Compared with Collagen Tile Brachytherapy	• GammaTile • Stereotactic radiosurgery	Phase 1
	Glioblastoma		
2	An Open-Label, Phase 1/2A Dose Escalation Study of Safety and Efficacy of NEO100 in Recurrent Grade IV Glioma	• Perillyl alcohol (inhaled)	Phase 1/2A
3	A Phase 1/2 Study of Selinexor and Temozolomide in Recurrent Glioblastoma	• Selinexor + Temozolomide • Temozolomide	Phase 1/2
4	Testing the Addition of the Immune Therapy Drugs, Tocilizumab and Atezolizumab, to Radiation Therapy for Recurrent Glioblastoma (BN010)	• Radiation + Tocilizumab + Atezolizumab • Radiation + Tocilizumab	Phase 2
5	Multi-Center Randomized Controlled Phase 2b Clinical Trial to Evaluate the Safety and Efficacy of TVI-Brain-1 Combined with Conformal Radiotherapy and Temozolomide Compared to Standard Therapy as a Treatment for Newly Diagnosed O6-Methylguanine Methyltransferase Negative (MGMT Unmethylated) Grade 4 Astrocytoma (GBM)	• TVI-Brain-1 + Radiation + Temozolomide • Standard therapy	Phase 2b
6	GammaTile and Stupp in Newly Diagnosed GBM (GESTALT)	• GammaTile + Standard therapy • Standard therapy	Phase 4
	Meningioma		
7	An Open-Label, Phase 2 Study of NEO100 in Participants with Residual, Progressive or Recurrent High-grade Meningioma	• Perillyl alcohol (inhaled)	Phase 2
8	Observation or Radiation Therapy in Patients with Newly Diagnosed Grade II Meningioma That Has Been Completely Removed by Surgery (NRG-BN003)	• Radiation • Standard therapy	Phase 3

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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**