BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

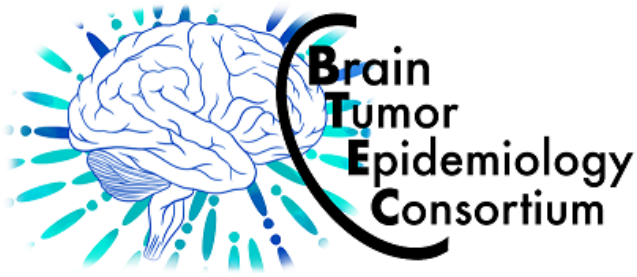
Mainz – Germany

May 15-17, 2024

BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

Funding for this conference was made possible (in part) by 1R13CA290955-01 from the National Cancer Institute.



The Brain Tumor Epidemiology Consortium (BTEC) is dedicated to the open exchange of ideas, and freedom of thought and expression. We are committed to running a successful meeting that fosters collegiality and celebrates diversity. The aims and goals require an environment that recognizes the inherent worth of every person and group, that fosters dignity, understanding, and mutual respect, and that embraces diversity.

To help ensure these goals, each presenter, speaker, and attendee must adhere to the following code of conduct. The expected behavior extends to all sessions, activities, events, and informal gatherings during the conference and to any other activities, in person or virtual, sponsored or managed by BTEC. Participants who do not comply may be barred from attending the remainder of BTEC events or barred from participating in other BTEC activities or meetings, in person or virtual.

General Behavior: Participants are expected to respect one another and behave in a civil fashion. Members should respect common sense rules for public behavior, personal interaction, common courtesy, and respect for all meeting participants.

Anti-Discrimination: BTEC prohibits discrimination at its meeting against individuals on the basis of factors such as race, ethnicity, color, sex, sexual orientation, gender identity or expression, age, marital status, religion, national origin, ancestry, socio-economic status, physical appearance, or different abilities.

Anti-Harassment: To promote an environment that recognizes the inherent worth of every person and group, BTEC is dedicated to providing its members and meeting attendees a harassment-free experience. Harassment is unwelcome or hostile behavior, including speech that intimidates or interferes with a person's participation or opportunity for participation in a conference, event, or program. Harassment in any form, including but not limited to, harassment based on national origin, race, religion, sex, gender, or any other status protected by laws in which the conference or program is being held, will not be tolerated. Harassment includes the use of abusive or degrading language or gestures, intimidation, stalking, harassing photography or recording, inappropriate physical contact, and unwelcome sexual attention.

Other unacceptable behavior includes, but is not limited to:

- Publicly sharing screen shots, photographs, video, or audio recording of oral or poster presentations, slides, or question periods without the consent of presenters and/or contributors.
- Making BTEC resources available to others outside one's immediate laboratory when membership or registration is required for access. When participating in events, in-person or virtual, attendees must use their own name and not attempt to misrepresent themselves in any way.
- Collecting data without ensuring protocols are in accordance with governing ethical and legal standards.
- Fabrication or misrepresentation of data presented at the conference.
- Verbal or written comments, or visual images, that are sexually suggestive, or that denigrate or show hostility or aversion toward an individual, or group of individuals, or that create an intimidating,

hostile, or offensive environment, or that unreasonably interfere with an individual's ability to participate in the event.

- Unwelcome sexual advances or touching, requests for sexual favors, or other unwelcome physical, verbal, visual, or other conduct of a sexual nature.
- Inappropriate use of nudity, sexual images, or images that would be reasonably found offensive by the membership.
- Real or implied threat of professional or financial damage or harm.
- Sustained or repeated disruption of talks or other events,
- Failing to stop unacceptable behavior when requested by a participant or BTEC representative.

An attendee whose safety is threatened or violated is urged to contact local law enforcement immediately. In addition, any attendee who feels unsafe or experiences unwelcome conduct, who observes or experiences unacceptable behavior, or who believes there has been a violation of the Code of Conduct Policy, are encouraged to report the matter to a BTEC board of directors member. Alternatively, a report may be made on the BTEC website at https://sites.usc.edu/braintumorcause/contact-usdonations/. Reports may be anonymous or attributed. Any reports will be handled in the strictest confidence. BTEC will respond promptly, including by offering supportive measures, informing parties about the available complaint and investigation processes, and taking reasonable care to prevent and promptly correct discrimination or harassment.

A review committee consisting of the meeting host and board of directors will confidentially adjudicate any reports, based on interviews of those making the report, those accused in the report, and witnesses to the event(s). Speech or contact determined to violate BTEC polides will be will be adjudicated as one of three types: (i) first event requiring discussion/corrective action; (ii) second event; (iii) event of a most serious nature. Events of type (i) will lead to a discussion by the committee with the individual and indication that such behavior is not acceptable. Events of types (ii) and (iii) will lead to expulsion from the conference. Events of type (iii) may, at the discretion of the review committee, also be referred to local authorities. The home institution or employer may be informed of allegations against or violations by faculty members, trainees, and affiliates.

Individuals may also notify NIH (https://public.era.nih.gov/shape/public/notificationForm.era or 301-480-6701) or file a complaint with HHS OCR at the address below about concerns of harassment, including sexual harassment, discrimination, and other forms of inappropriate conduct at NIH-supported conferences.

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
800-368-1019, 800-537-7697 (TDD)
https://www.hhs.gov/ocr/complaints/index.html

Filing a complaint with BTEC is not required before filing a complaint of discrimination with HHS OCR, and seeking assistance from BTEC in no way prohibits filing complaints with HHS OCR.

The **Brain Tumor Epidemiology Consortium (BTEC)** is an open scientific forum organized to foster the development of multi-center, international and inter-disciplinary collaborations that will lead to a better understanding of the etiology, outcomes, and prevention of brain tumors. During the process of attaining this mission, BTEC members mentor junior investigators or investigators who are new to brain tumor epidemiologic research. Depending on funding, young investigators awards are given during the BTEC annual meetings.

The Consortium was formed in 2003 after an initial meeting sponsored by the National Cancer Institute's (NCI) Division of Cancer Epidemiology and Genetics (DCEG), which is the intramural (in house) research component of the Institute, and the National Institutes of Health's (NIH) Office of Rare Diseases (ORD), and has evolved as a self-directed consortium. BTEC members have formed several Working Groups developing ideas for coordinated research focusing on adult gliomas, meningiomas, pediatric brain tumors, and family-studies.

The **BTEC Board of Directors** consists of members and officers selected to represent the BTEC members. The group meets monthly via teleconference. Full listing here.

BTEC holds annual meetings and webinars to discuss current and future collaborations and scientific findings.

BTEC meetings are the only yearly meetings that focus solely on the etiology and epidemiology of brain tumors. These meetings provide an opportunity for international researchers to exchange ideas and form novel collaborations. These forums also provide an opportunity for mentoring young investigators studying these tumors.

BTEC is a National Cancer Institute designated consortium. BTEC is a non-profit 501(c)(3) corporation. BTEC's mission is only to facilitate collaborative research; we are not a lobbying or advocacy organization.

BTEC website: https://sites.usc.edu/braintumorcause/

Brain Tumor Epidemiology Consortium Mentoring Fellowship

The Brain Tumor Epidemiology Consortium (BTEC) Mentoring Executive Committee is seeking applicants for fellowship training in brain tumor epidemiologic and clinical research. Applicants should have an MD or PhD in Epidemiology, Biostatistics, Health Behavior, or related area of health or basic sciences and interest in receiving applied training and mentorship in brain tumor epidemiology. Qualified candidates should have access to an existing data set and have a research question of interest in process or with data for development. Fellowships will be awarded for a 1-year window, during which time fellows will receive mentorship on the development, biostatistical analysis, and writing of a manuscript appropriate for submission and publication in a prominent, peer-reviewed, health research journal. All fellows will be matched with a primary, academic mentor from the BTEC membership with international research experience in brain tumor epidemiology and successful publication record. The fellow will also receive advisement and assistance from a committee including academic mentors from clinical medicine, biostatistics, and epidemiology. Fellows will be expected to develop a research article in the theme of brain tumor epidemiology or clinical research for publication with guidance from their committee. Fellows with a successful abstract submission to the BTEC annual meeting will also receive BTEC membership and registration to present at the annual BTEC consortium meeting in 2025.

Interested applicants may send a copy of their curricula vitai, 1 page description of their research interests and desired areas of training and mentoring, and 1 page description of their available data and proposed research question. Applications are requested by September 1, 2023 and may be submitted to:

BTEC Mentoring Fellowship Executive Chairs:

Ching Lau, M.D, Ph.D, Martin J Gavin Endowed Chair and Head of the Division of Hematology and Oncology, Connecticut Children's Medical Center, Professor of the Jackson Laboratory and University of Connecticut School of Medicine. ching.lau@jax.org

Roberta McKean-Cowdin, PhD, Professor Keck School of Medicine of the University of Southern California, Department of Population and Public Health Science, Norris Comprehensive Cancer Center mckeanco@usc.edu

More information about BTEC may be found at BTEC members – Brain Tumor Epidemiology Consortium (usc.edu) and Research Consortia & Collaborative Research Groups | EGRP/DCCPS/NCI/NIH (cancer.gov)

Meeting Location:

Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI)
Rhabanusstraße 3
55118 Mainz

Meeting room: 21.9 (Tower A, 21st floor)

BTEC Conference coordinator:

Bénédicte CLEMENT - Cell: +33 6 10 25 38 96 - email: benedicteclement2507@gmail.com

BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

BTEC would like to thank the American Brain Tumor Association for its support of the 2024 BTEC annual meeting, especially for its generous and continued support of our Junior Investigators.

The mission of the American Brain Tumor Association is to advance the understanding and treatment of brain tumors with the goals of improving, extending and, ultimately, saving the lives of those impacted by a brain tumor diagnosis.

We do this through interactions and engagements with brain tumor patients and their families; collaborations with allied groups and organizations; and the funding of brain tumor research.

For more than 50 years, the American Brain Tumor Association has served as the champion of the brain tumor community, providing comprehensive resources to support the complex needs of brain tumor patients and caregivers, across all ages and tumor types, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnoses, treatments and care.

The American Brain Tumor Association provides:

INFORMATION

The ABTA website (www.abta.org) offers more than 200 pages of information, programs, support services and resources, including brain tumor treatment center and support group locators, caregiver resources, research updates and tumor type and treatment information across all ages and tumor types.

EDUCATION AND SUPPORT

- **ABTA Educational Meetings & Webinars**
  - In-person and virtual educational meetings and webinars led by nationally-recognized medical professionals.

- **ABTA Patient and Caregiver Mentor Support Program**
  - Connect with a trained patient or caregiver mentor to help navigate a brain tumor diagnosis

- **ABTA Connections Community**
  - An online support and discussion community of more than 30,000 members

- **ABTA Educational Brochures**
  - Educational brochures on a range of topics are available on our website or can be requested in hard copy format for free by calling the ABTA

- **ABTA CareLine**
  - For personalized information, resources and support call 800-886-ABTA (2282) or email abtacares@abta.org to connect with a CareLine staff member.

RESEARCH FUNDING

Since 1976, the ABTA has awarded more than $35 million in research grants supporting early-career investigators, contributing to the modern brain tumor research and scientific community to advance the field's scientific understanding and medical treatment of brain tumors. Today, the ABTA's research alumni are leading some of the nation's most prestigious brain tumor centers and serving as mentors to a new generation of scientists.

An independent, multi-level review process ensures that ABTA grants are awarded for the most meritorious brain tumor research projects. Through the funding of research, ABTA supports projects that will change our understanding of the causes, effects, diagnosis, and treatment of brain tumors. We fund innovative discovery science that is developing new drugs, new imaging techniques, and advanced methods of diagnosis as well as research that will improve the quality of life of brain tumor patients and their caregivers.

American Brain Tumor Association
8550 W. Bryn Mawr Ave., Suite 550
Chicago, IL 60631

Toll-Free: 800-886-ABTA (2282)
Email: info@abta.org
Web: **www.abta.org**

BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

BTEC would like to thank the Uncle Kory Foundation for its unrestricted contribution to the meeting.

Uncle Kory FOUNDATION

We've got brain cancer surrounded.

Uncle Kory FOUNDATION

We've got brain cancer surrounded.

The Uncle Kory Foundation's mission is to advance innovative and collaborative brain cancer research to specifically improve the survival rate and treatment of those diagnosed with brain cancer. To date, UKF has donated over $3.6 million dollars to brain cancer research globally for pediatric and adult brain tumor research.

More information here: www.unclekory.org

UNCLE KORY SEED GRANT PROGRAM

2024 Seed Grant Program

The Uncle Kory Foundation (UKF) Seed Grant Program is designed to allow Research Investigators to apply for much needed resources to begin or continue their research as it relates to brain cancer, and when possible, specifically Glioblastoma. The seed grants from UKF are established at $50,000 for the first year and $50,000 for the second year, if renewed. UKF grants do not include funds for institutional overhead.

.

APPLICATION DATES

Application Period: September 1, 2024 – October 1, 2024
Application Deadline: October 1st, 2024
Medical Advisory & Board Decision: After November 30th, 2024
Funding Available: After December 15th, 2024

More information here: https://www.unclekory.org/grant-details

BTEC 2024 Annual Conference

AGENDA

Wednesday, May 15	
4:30 – 5:30 pm 6:00 – 8:00 pm	Sightseeing Train Tour Cocktail reception and local introductions
Thursday, May 16	
7:30–8:00 am	Welcome coffee and badge pick-up
8:10–8:30 am	**Welcome Remarks** Michael Scheurer, Yan Yuan, Friederike Erdmann, Cecile Ronckers
8:30–10:00 am	**Session 1 – Chairs:** Michael Scheurer, Friederike Erdmann
8:30–9:00 am	**Keynote lecture: Survival Trends for brain tumors** *Fabio Girardi, London School of Hygiene and Tropical Medicine - UK*
9:00–9:30 am	**Keynote lecture: Current topics in late effects of childhood brain tumor therapy** *Paul Nathan, University of Toronto/Sick Kids-Canada*
9:30–10:00 am	**Keynote lecture: Understanding the health issues of adult brain tumor survivors** *Florien Boele, Leeds Institute of Health Sciences – UK*
10:00–10:30 am	**Abstract presentations** **Chairs:** Johannes Hainfellner and Yan Yuan
10:00 – 10:15 am	**Survival patterns of pediatric central nervous system tumors in Germany 1980-2016: a nationwide assessment based on data from the German Childhood Cancer Registry** *Maike Wellbrock*, *Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI), Mainz – Germany*
10:15 – 10:30 am	**Epidemiology, clinical data and long-term functional outcomes for operated central neurocytoma patients: preliminary results of the French experience** *Luc Bauchet, CHU Montpellier, Montpellier - France*

10:30–11:00 am	Coffee Break
11:00–12:00 am 11:00–11:30 am 11:30–12:00 am	**Session 2** Chairs: Luc Bauchet, Michael Scheurer **Keynote lecture: Psychosocial and mental health outcomes among cancer survivors** *Andrea Pace, IRCCS Regina Elena National Cancer Institute - Italy* **Keynote lecture: Dealing with disability as a brain tumor survivor** *Kiri Ness, St. Jude Children's Research Hospital-USA*
12:00–1:15 pm	Lunch and BTEC Advisory Board Meeting
1:15 – 3:30 pm 1:15– 1:30 pm 1:30 –1:45 pm 1:45 – 2:00 pm 2:00 – 2:15 pm 2:15 – 2:30 pm 2:30 – 3:30 pm 2:30 – 3:00 pm REMOTE 3:00 – 3:30 pm	**Abstract presentations (Remote Sessions presented Live via Zoom)** *Chairs: Quinn Ostrom, Ching Lau* **Standard of care for follow up for neurovascular late effects after radiotherapy for pediatric brain tumors** *Louise Tram Henriksen, Aarhus University Hospital, Aarhus - Denmark* **The Epidemiology of CNS Tumors in Arab Countries: A Globocan Database Analysis** *Sarah Al Sharie, Faculty of Medicine, Yarmouk University, Irbid - Jordan* **International Benchmarking of Childhood Cancer Survival by Stage (BENCHISTA Project): Results for medulloblastoma** *Angela Lopez-Cortes, University College London – UK* **Temporal Variation in Glioblastoma Multiforme Across the United States: Incidence Increases from 2000 to 2017** *Syed A. Sarwar, Jersey Shore University Medical Center, Neptune, NJ – USA* **Impact of Maternal Health and Demographics on Childhood Brain Tumor Incidence: An Epidemiological Study** *Julia Botvinov, Hackensack Meridian School of Medicine, Nutley, NJ – USA* **Session 3** *Chairs: Scott Coven, Carol Kruchko* **Keynote lecture: Social determinants of brain tumor survivorship** *Vidya Puthenpura, Yale University, New Haven, CT – USA* **Keynote lecture: Financial toxicity among brain tumor survivors** *Nicole Willmarth, American Brain Tumor Association, Chicago, IL – USA*
3:30–4:00 pm	**Coffee break**
5:30 pm	**Meeting in front of the Me and Mainz Hotel** **Sparkling wine tour and conference dinner (additional registration was required)**

Friday, May 17	
8:00 –8:30 am	**Welcome coffee**
8:30 -9:30 am 8:30 –9:00 am 9:00–9:30 am 9:30–10:00 am 9:30 – 9:45 am 9:45 – 10:00 am	**Session 4** *Chair:* Roberta McKean-Cowdin **Keynote lecture: Using machine learning and AI to predict brain cancer survival** *Annette Molinaro, UCSF, San Franciso, CA - USA* **Brain tumor classification by enzymatic DNA methylation sequencing of cell free DNA from cerebrospinal fluid** *Ching Lau, The Jackson Laboratory, Farmington, CT - USA* **ABTA Junior Investigator Awardees** *Introduction by Michael Scheurer and Yan Yuan* **US- Junior Investigator Award Winner** **Novel Susceptibility Variants in Adult and Pediatric Ependymoma** *Joshua D. Strauss, Baylor College of Medicine, Houston, TX - USA* **Non-US- Junior Investigator Award Winner** **Geographical Survival Comparison and Estimated Long-Term Survival Outcomes of Pediatric CNS Tumors from 31 European Countries – Results from the Population-Based EUROCARE Project** *Raoull Hoogendijk, Princess Máxima Center for Pediatric Oncology, Utrecht -The Netherlands*
10:00–10:30 am	**Coffee break**
10:30 – 10:45 am 10:45 – 11:00 am 11:00 – 11:15 am 11:15 – 11:30 am	**Abstract presentations** **Chairs:** *Ching Lau, Luc Bauchet* **Enrichment of a neutrophil-like monocyte transcriptional state in glioblastoma myeloid suppressor cells** *Emily Nissen, University of Kansas Medical Center, Kansas City, KS – USA* **Establishing a "Medical Home" for Children with Incidental Brain Lesions** *Scott L. Coven, Riley Hospital for Children at IU Health, Indianapolis, IN – USA* **Association between congenital anomalies and childhood brain tumors in 22 million live births** *Thanh T. Hoang, Baylor College of Medicine, Houston, TX - USA* **Multiscale Geographically Weighted Linear Regression for County-Level Glioblastoma Incidence Modeling in the United States** *Mackenzie Price, Central Brain Tumor Registry of the United States, Hinsdale, IL – USA*

11:30 – 11:45 am	**Investigating Diagnostic Cost Disparities for Central Nervous System Tumours Across Canadian Provinces** *Yan Yuan, University of Alberta, Alberta – Canada*
11:45 – 12:00 pm	**Investigating the Role of Germline DNA in the Brain Location of Adult Glioma Tumors** *Karen Alpen, University of Melbourne, Melbourne - Australia*
12:00–1:30 pm	**Lunch and BTEC Business Meeting**
1:30–2:15 pm	**Abstract presentations** **Chairs:** *Friederike Erdmann, John Villano*
1:30 – 1:45 pm	**Parental occupational exposures and de novo neurocutaneous syndromes in the offspring: findings from a register-based Swedish case-control study** *Christina-Evmorfia Kampitsi, Karolinska Institutet, Stockholm – Sweden*
1:45 – 2:00 pm	**Characteristics of Mental Health Disorder Among Central Nervous System Cancer and Other Childhood Cancer Patients – A Population-based Study for Medicaid Beneficiaries in Kentucky** *Bin Huang, University of Kentucky, Lexington, KY - USA*
2:00 – 2:15 pm	**Characterization of novel multi-target compounds for the treatment of glioblastoma** *Aizpea Artetxe Zurutuza, Biogipuzkoa Health Research Institute, San Sebastian - Spain*
2:15 – 2: 30 pm	**Descriptive epidemiology of Childhood Primary Brain Tumors in Uganda: Data from a Tertiary Center** *Victoria Mwebe Katasi, Mulago National Referral Hospital, Kampala - Uganda*
2:30 – 2:45 pm	**Long-term antidepressant drugs use among Childhood CNS Tumor Survivors in Sweden: a register-based cohort study** *Javier Louro, Karolinska Institutet, Stockholm - Sweden*
2:45 – 3:15 pm	**Coffee break**
	Abstract presentations (continued) **Chairs:** *Friederike Erdmann, John Villano*
3:15 – 3:30 pm	**The effect of prior varicella zoster infection on a person's risk of glioma development** *Christine Ann Pittman Ballard, University of North Carolina, Chapel Hill, NC - USA*
3:30 – 3:45 pm REMOTE	**Maternal exposure to solvents from industrial sources during pregnancy and childhood cancer risk in California** *Stephanie Chen, UCLA, Los Angeles, CA – USA*
3:45–4:00 pm REMOTE	**Sex Differences in Adverse Events Post Treatment in Glioblastoma** *Mantas Dmukauskas, National Cancer Institute, Bethesda, MD - USA*
4:00 – 4:15 pm REMOTE	**De novo replication repair deficient glioblastoma, IDH-wildtype" is a distinct glioblastoma subtype in adults that may benefit from immune checkpoint blockade** *Sara Hadad, University of California San Francisco, San Francisco, CA - USA*

Social events at BTEC

Wednesday, May 15

4:30 – 5:30 pm – Sightseeing Tour with Mainz Touristic Train (additional registration was required)

Join us for a **50-minute sightseeing tour** on board the Gutenberg-Express to visit the most important attractions of Mainz.

We will pass narrow lanes, look at beautiful civil houses, especially the **CATHEDRAL**, **St. STEPHAN**, the **CITADEL**, the **ELECTORAL PALACE**, the **PARLIAMENT** und the **NEW SYNAGOGUE** and admire several Roman buildings and buildings of the middle age.

6:00 – 8:00 pm – BTEC Welcome Cocktail Reception (included in meeting registration)

Location: Me and Mainz Hotel

Join us for this casual get together and pick up your delegate material.

Thursday, May 16 (additional registration fees required 85$ - 55$)

5:30pm: Champagne Winery Tour


Join us for a tour of a local champagne winery including a tasting of 2 different sparkling wines.

7:15 pm: Group Dinner


Join us for a typical 3-course dinner of the region Rhine Hesse (vegetarian option available – Vegan option upon request) with a selection of local wines.

AGENDA BTEC Business Meeting

Friday, May 17, 12:30-1:45 pm (lunch)

The Brain Tumor Epidemiology Consortium (BTEC) is a self-directing consortium committed to developing multi-center, interdisciplinary collaborations that will lead to a better understanding of the etiology of brain tumor development and outcomes.

Co-Presidents:	Michael Scheurer **(2022-2024)** Yan Yuan **(2023-2025)**
Co-Vice Presidents:	Roberta McKean-Cowdin **(2022-2024)** Jon Foss-Skiftesvik **(2023-2025)**
Secretary:	*vacant*
Treasurer:	Quinn Ostrom (**2020-2024**)

The Consortium is grateful to the American Brain Tumor Association, the Uncle Kory Foundation and the US National Cancer Institute for providing funding for the 2024 BTEC Meeting in Mainz, Germany.

Business Meeting Agenda

1. **Administrative Update……. Michael Scheurer & Luc Bauchet**
    a. **Funding Support & Acknowledgement**
    b. **Financial Report…… Quinn Ostrom**
2. **Nominations/Voting ……. Roberta Mckean-Cowdin & Yan Yuan**
    a. **Nomination slate**
        1. US Vice-President: Stephen Francis
        2. Secretary: Christine Ballard
        3. Treasurer: Thanh Hoang
        4. Nominations from floor
        5. Voting will occur via email after the meeting
3. **BTEC Mentor Program…… Ching Lau & Roberta McKean-Cowdin**
4. **BTEC Webinar Program……. Quinn Ostrom & Stephen Francis**
5. **Service Awards……. Michael Scheurer**
6. **Co-Presidents Comments…… Michael Scheurer & Yan Yuan**
7. **Future Meetings……. Michael Scheurer**
8. **Discussion from the Membership**

Candidate Statements for Board Positions

US Vice-President: Stephen Francis, PhD

I am an Associate Professor in the Department of Neurological Surgery at UCSF, where I am a computational and molecular epidemiologist. Much of my work centers around immune priming exposures, such as common infections and allergy, and how these exposures influence glioma risk and survival and interact with germline and somatic genetics. I have served on the BTEC board for the last 3 years and I am excited to continue contributing to the group through this leadership position.

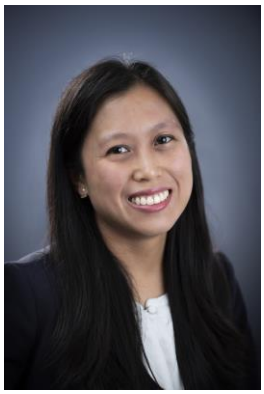
Secretary: Christine Ballard, PhD

I have over a decade of experience in neuro-oncology epidemiology, as an researcher at the University of Rochester and now Duke University. Currently I am pursuing a PhD in Epidemiology at the University of North Carolina Chapel Hill, where my research focuses on the convergence of pharmacoepidemiology, genomic epidemiology, and brain tumors.

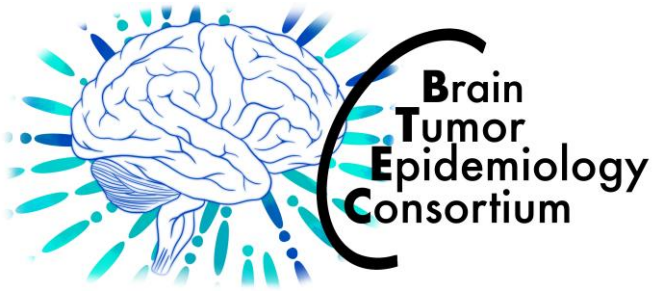
As a candidate for the role of Secretary at the Brain Tumor Epidemiology Consortia (BTEC), I am committed to fostering collaborative research efforts. I am particularly passionate about engaging the next generation of researchers and am eager to work with BTEC to develop strategies for involving more student researchers in this field.

It would be an honor to contribute to BTEC's mission.

Treasurer: Thanh Hoang, PhD



Dr. Thanh Hoang is an Assistant Professor at Baylor College of Medicine. Her research interests are to better understand the role of molecular biology and environmental factors on the development of pediatric cancers, including brain tumors, and their association with treatment outcomes. Dr. Hoang has experience managing the budget of a pilot award and NIH supplemental award and enjoys filing her taxes each year.



BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

Keynote speakers

Florien Boele, BSc, MSc, PhD, FHEA

Dr Florien Boele is an Associate Professor of Medical Psychology at the University of Leeds. Dr Boele has a background in neuropsychology and obtained her PhD from the VU University Medical Center in Amsterdam (2015). She leads a small research group which focuses on health-related quality of life and (access to) support in (neuro-)oncology patients and family caregivers. Dr Boele is involved in several clinical trials as patient-centered outcomes expert.

In addition, Dr Boele is an active member of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group, and the European Association of Neuro-Oncology (EANO). She currently chairs the EANO Nurse & Allied Health Professionals Committee. She is involved in several international initiatives such as the Response Assessment in Neuro Oncology (RANO) – Cares working group, the International Neuro-oncology Caregiver Consortium (INCC), and the Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials – IMI (SISAQOL-IMI) consortium.

From 2024, next to her academic role at the University of Leeds, Dr Boele has taken up a role at the Dutch Cancer Society to help guide the long-term quality of life research funding strategy.

Fabio Girardi, MD, PhD

I am a practicing medical oncologist and epidemiologist. After completing my medical training in Padova (Italy), I worked for several years as a consultant, mostly in community hospitals. I became progressively aware of disparities in access to cancer care and committed to addressing such disparities through research.

In 2015 I moved to the UK to embark on an MPhil in Epidemiology at the University of Cambridge, and, in 2017, on a funded PhD with the Cancer Survival Group at the London School of Hygiene and Tropical Medicine. Here I contributed to the CONCORD program for the global surveillance of population-based cancer survival, led by Prof Claudia Allemani and Prof Michel P Coleman.

During my PhD, I had the privilege of joining the Lancet Oncology Commission on Sustainable Care for Children with Cancer as a member of the core analytic team. For the Commission, I defined the epidemiological framework and produced new survival analyses. These analyses were the foundation for modelling studies aimed at informing the Commission's case for investment in childhood cancer control and were included in a landmark, highly cited publication.

I was awarded my PhD in April 2021 with the thesis, "Global surveillance of survival from intrinsic brain tumors diagnosed during 2000-2014: trends by age and histology", and went on to collaborate with the Cancer Survival Group as a Honorary Clinical Assistant Professor in Cancer Epidemiology.

In 2020 I relocated to my home country to take on a post as senior consultant medical oncologist at the Istituto Oncologico Veneto (IOV-IRCCS) in Padova, the tertiary cancer referral centre for the northeast of Italy. Here I have been appointed Adjunct Professor of Oncology at the University of Padova.

Paul Nathan, MD

Dr. Paul Nathan is Director of the AfterCare clinic and the Section Head of the Solid Tumor section in the Division of Pediatric Hematology/Oncology and a Senior Associate Scientist in the Research Institute at the Hospital for Sick Children. He is a Professor of Pediatrics and Health Policy, Management and Evaluation at the University of Toronto. Dr. Nathan completed his medical degree in 1991 from the University of Toronto. His research is focused on health care utilization by adult survivors of childhood cancer, as well as specific “late effects” of cancer therapy, including cardiac disease and second malignant neoplasms. He is a member of the American Society of Clinical Oncology, the Children’s Oncology Group, and the International Society of Pediatric Oncology (SIOP), as well as clinical committees focused on research, clinical care, and policy creation for long-term survivors of childhood cancer.

Kiri Ness, PT, PhD

Dr. Kirsten Ness is a physical therapist, clinical epidemiologist, and a Member in the Department of Epidemiology and Cancer Control at St. Jude. In her research work, she focuses on recognizing, describing, and remediating functional limitations in childhood cancer survivors. As Principal Investigator of the Human Performance Lab at St. Jude, Ness collaborates with other investigators to understand physiological impairments and problems with movement and physical function in patients and survivors of childhood cancer. She serves on the Executive Committee of the Childhood Cancer Survivor Study and the Children's Oncology Group Long Term Follow-up Guidelines for Survivors of Childhood and Adolescent Cancer. She is an active member of the Survivorship and Outcomes Committee at the Children's Oncology Group, and serves on the Editorial Boards of Physical Therapy and the Journal of Cancer Survivorship. Dr. Ness teaches the Introduction to Epidemiology Course in the St. Jude Graduated School of Biomedical Sciences. She also serves on several editorial boards and teaches the Introduction to Epidemiology course within the St. Jude Graduate School. In 2023, her leadership and commitment to the field of public health was recognized with the Gaylord Anderson Leadership Award, presented to an alumnus of the University of Minnesota School of Public Health.

Andrea Pace, MD

Dr Andrea Pace is a neurologist, chair of the Neuro-Oncology Unit at the Cancer Institute Regina Elena in Rome, Italy. His research interest is focused on Brain Tumor treatment, supportive and palliative care. He has also a strong interest in clinical research on neurological complications of cancer treatments, particularly on peripheral nerve neurotoxicity and cognitive neurotoxicity.

He is author of 190 peer reviewed scientific papers.

Vidya Puthenpura, MD, MHS,

Vidya Puthenpura, MD, MHS, is a pediatric hematologist and oncologist who says she seeks a strong connection with her patients and families.

“I love my patients and I’m really attached to them,” she says. “A cancer diagnosis is hard and one thing that can ease their mind is knowing that I am there for them through both the good and tough times. I find I do my best work when I am emotionally connected to what I do, and having that connection with children and their families is so rewarding.”

Dr. Puthenpura originally thought she wanted to be an engineer, but a volunteer experience she had at a pediatric cancer institute convinced her she wanted to be a doctor and work with kids.

“The children were so amazing and motivated and I knew I wanted to help them get better,” she says. “In medical school, I explored a few different specialties, but I kept coming back to hematology and oncology. I love that you have continuity of care because you spend so much time with patients and make a connection. I also loved that the field is constantly growing and changing with innovations.”

Dr. Puthenpura treats a variety of conditions, but her personal area of interest is in pediatric brain tumors.

“We have an amazing multidisciplinary team. Our goal is to focus on the entire family, including caregivers and siblings,” she says. “We tailor how we explain what is going on to a child based on their age and level of maturity. And for parents, we try to explain things in a thorough manner because we need them to understand what is going on. For some, we break it down into parts, whereas other parents come in armed with information about clinical trials.”

Her research examines health disparities. “Adolescents and young adults in the U.S. who have brain tumors and are minorities and live in rural areas are disadvantaged—and tend to have decreased survival rates and access to clinical trials compared to non-Hispanic, white youth,” she says. “These issues are important, and I’m happy to see them coming to the limelight more.”

Nicole Willmarth, PhD

Nicole Willmarth joined the American Brain Tumor Association (ABTA) in 2015. In her role as Chief Mission Officer, she has oversight of the strategic direction, expansion and operation of the ABTA's research grants, patient support, education and awareness. She leads a team in developing and executing ABTA's investment toward the mission to improve the lives of people living with a brain tumor. Prior to joining ABTA, Nicole served in a leadership position at Susan G. Komen® where she oversaw the business and science management of Komen's portfolio of funded research program grants. She worked with patient advocates as well as a team of science managers and grant administrators to ensure the organization's research investment aligned with the mission and maximized potential to advance the field. Nicole began her career in scientific grant management with the American Association for Cancer Research (AACR). She developed, launched and managed several grant mechanisms as part of AACR's donor-directed research grants programs and provided oversight for the application and scientific review process and science management. She also managed AACR's Scholar-in-Training Awards, the Associate Member Council and the Molecular Epidemiology Working Group. Nicole is currently a member of several organizations and committees including the Society for Neuro-Oncology (SNO), the National Comprehensive Cancer Network (NCCN) Guidelines Panel for Central Nervous System Cancers and the National Institute's (NCI) National Council of Research Advocates. Nicole was the 2021 recipient of SNO's Jan Esenwein Public Service Award. Nicole received her Ph.D. in Cellular and Molecular Biology at the University of Michigan where she first developed her passion for advancing treatments in the cancer field. She went on to publish in a number of peer reviewed scientific journals over the course of a decade in research. She currently resides in Chicago, Illinois

BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

Junior Investigator Awards

Supported with a generous grant from

the American Brain Tumor Association

US JUNIOR INVESTIGATOR AWARDEE

Joshua Strauss

EDUCATION
University of Texas, Houston, TX August 2023 – Current
•Doctor of Philosophy in Epidemiology

University of Pittsburgh, Pittsburgh, PA April 2023
•Master of Public Health in Epidemiology

Binghamton University, Binghamton, NY January 2018
•Bachelor of Science in Cell Molecular Biology

RESEARCH PRACTICUM
National Cancer Institute – Clinical Genetics Branch May 2022 – August 2022
Summer Research Fellow; Senior Investigator - Shahinaz Gadalla, MD, PhD; Derek Brown, PhD
•Statistical analysis of severe aplastic anemia patients undergoing transplantation
•Creation and presentation of research poster•Manuscript submission pending

PROFESSIONAL EXPERIENCE

August 2022 – Current
Baylor College of Medicine – Center for Epidemiology and Population Health
Research Assistant II

August 2022 – April 2023
National Cancer Institute – Clinical Genetics Branch August 2022 – April 2023
Special Volunteer

July 2020 – July 2021
Franciscan Health
Clinical Research Coordinator II

August 2019 – June 2020
Vanderbilt University Medical Center
Clinical/Translational Research Coordinator II

March 2018 – July 2019
Maryland Proton Treatment Center
Medical Physicist Extender

BENCH RESEARCH EXPERIENCE

May 2018 – August 2019
University of Maryland Baltimore, School of Medicine
Research Associate; Dr. Zeljko Vujaskovic, Radiation Oncology Lab

Novel Susceptibility Variants in Adult and Pediatric Ependymoma

Joshua D. Strauss[1-3], Priya B. Shetty[4,5], Spiridon Tsavachidis[4,5], Jinyoung Byun[4-6], Stephen C. Mack[7], Xiao Xiangjun[4-6], Terri S. Armstrong[8], Mark R. Gilbert[8] (on behalf of NCI-Connect), Lisa Mirabello[9], Smita Bhatia[10], Wendy M. Leisenring[11], Lindsay M. Morton[12], Gregory T. Armstrong[13], Jon Foss-Skiftesvik[14,15], Christian Munch Hagen[15], iPSYCH Consortium[16], Jonas Bybjerg-Grauholm[15], Manel Ghozal[17], Audrey Bonaventure[17], Jacqueline Clavel[17, 18], Melissa L. Bondy[19] (on behalf of GICC), Christopher I. Amos[4-6], Michael E. Scheurer[1-5]

1. Center for Epidemiology and Population Health, Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA
2. Department of Pediatrics, Section of Hematology-Oncology, Baylor College of Medicine, Houston, Texas, USA
3. Texas Children's Cancer Center, Texas Children's Hospital, Houston, Texas, USA
4. Department of Medicine, Section of Epidemiology and Population Sciences, Baylor College of Medicine, Houston, Texas, USA
5. Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, Texas, USA
6. Institute for Clinical and Translational Research, Baylor College of Medicine, Houston, Texas, USA
7. Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis, Tennessee, USA
8. Center for Cancer Research, National Cancer Institute, Bethesda, Maryland, USA
9. Clinical Genetics Branch, National Cancer Institute, Rockville, Maryland, USA
10. O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama, USA
11. Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA
12. Radiation Epidemiology Branch, National Cancer Institute, Shady Grove, Maryland, USA
13. Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee, USA
14. Department of Neurosurgery, Rigshospitalet University Hospital, Copenhagen, Denmark
15. Danish Center for Neonatal Screening, Department of Congenital Diseases and Neonatal Genetics, Statens Serum Institut, Copenhagen, Denmark
16. The Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH)
17. Center for Research in Epidemiology and Statistics CRESS, Epidemiology of childhood and adolescent cancer team, University Paris Cité, University Paris Sorbonne Nord, INSERM, INRAe, Villejuif, France
18. National Registry of Childhood Cancer, Hôpital Paul Brousse, Groupe Hospitalier Universitaire Paris-Sud, Assistance Publique Hôpitaux de Paris (AP-HP), Villejuif, and Centre Hospitalier Régional Universitaire de Nancy, Vandoeuvre-lès-Nancy, France
19. Department of Epidemiology and Population Health, Stanford University School of Medicine, Stanford, California, USA

Background:

Ependymoma is a malignancy of the neuroepithelium that lines the spinal cord and ventricular system of the brain. Occurring in approximately two per million individuals annually, the rarity of ependymoma results in challenges for targeted research, underscoring the need to expand our comprehension of disease etiology and genetic risk.

Materials and Methods:

Our study included 543 ependymoma patients and 5,934 disease-free controls that provided blood or saliva samples for analysis from nine cohorts. All cohorts were phased and imputed based on the 1000 Genomes Phase 3 reference panel using BEAGLE 5.4. Imputed cohorts were merged into three analytic groups and underwent quality control filtering. These groups consisted of pediatric subjects with

whole genome sequencing (<18yrs old; 143 cases, 332 controls), pediatric subjects with genotyping (<18yrs old; 174 cases, 2340 controls), and adult subjects with genotyping (≥18yrs old; 226 cases, 3262 controls). Genome-wide association studies (GWAS) were conducted for each group, as well as a meta-analysis for the pediatric subjects and overall group using GMMAT. All models were adjusted for the first ten principal components to account for differences in ancestry between cases and controls. Significant alterations were defined as $p<5\times10^{-8}$.

Results:

Several overall and age-specific ependymoma risk loci were identified. Of note, significant pediatric variants were harbored on 1q34.2 (*CCDC30*), 7q21.3 (*DYNC1I1*), 11q13.4 (*SHANK2*), 12p13.2 (*PRR4*, *TAS2R14*), 12q23.1 (*LOC105369927*), 14q32.2 (Intergenic), and 15q11.2 (Intergenic). The pediatric meta-analysis further identified 10q11.22 as an intergenic locus. Adult ependymoma susceptibility variants were located on 1q34.2 (*CCDC30*), 4q35.2 (Intergenic), 7q31.31 (*LOC124901737*), 10p12.33 (*MRC1*), 11p15.4 (*TRIM66*), 15q11.1 (Intergenic), and 16q12.2 (*CES5A*). The overall meta-analysis identified several significant alterations to *CYFIP1* within the previously reported 15q11.2 locus.

Conclusions:

This study represents the largest ependymoma-specific GWAS to date. We identified several novel loci and genes not previously reported specifically for ependymoma risk. Although ependymoma consists of 10 distinct anatomic and molecular subtypes, alterations to *CCDC30*, a member of the cancer-associated CCDC family, were ubiquitous throughout adult and pediatric ependymoma, potentially representing a strong global risk factor. The pediatric GWAS identified significant variants within *SHANK2, DYNC1I1,* and *TAS2R14*. *SHANK2* is involved in post-synaptic scaffolding and has previously been linked to psychiatric disorders, cognitive impairment, and several cancers, such as neuroblastoma. Interestingly, *DYNC1I1* has also been identified as a tumor suppressor in glioblastoma, a brain cancer more common among older adults compared to ependymoma. *TAS2R14* is a known tumor suppressor and notably regulates resveratrol transmission across the blood-cerebrospinal fluid barrier. The adult GWAS found significant variants within *MRC1* (also known as *CD206*) and *TRIM66*, both of which have been associated with glioma. Finally, significant alterations to *CYFIP1* were able to be detected from the overall meta-analysis. *CYFIP1* has commonly been connected to epithelial cancers, in addition to the gene's association with psychiatric disorders and cognitive impairment. In conclusion, the genetic risk of ependymoma appears to be influenced by multiple loci and genes previously associated with neurologic diseases. The age-specific findings may permit further research into the etiological differentiation of ependymoma occurrence by age and potentially by molecular subtype.

NON-US JUNIOR INVESTIGATOR AWARDEE

Raoull Hoogendijk, PhD

Raoull Hoogendijk is a clinical epidemiologist finishing his PhD in cancer epidemiology, and starting his full-time postdoctoral research mid 2024. His overall research goal is to improve outcomes for children with a brain tumor. He has extensive experience in the analyses of low- and high-throughput biological data using advanced statistical methods. His research has a strong translational character with a focus on using observational data to improve treatment outcomes for pediatric brain tumors. His translational interest is reflected by his diverse involvement in multiple projects in the field of clinical trials, immunology, pathology, and microbiology. Currently, he is leading the analyses of the EUROCARE-6 data on pediatric CNS tumors (accompanying abstract attached). Lastly, he has a special interest in the role of the microbiome in pediatric brain tumors. His current microbiome investigations are part of the Monitor Immune Microenvironment and systemic immune effects in pediatric Brain tumors project (MIMIC study, https://clinicaltrialregister.nl/nl/trial/24486). He was recently awarded the Round III grant funding by the DIPG DMG Research Funding Alliance (DDRFA) as a co-investigator to study the microbiome in relation to treatment response and toxicity for the early phase pediatric neuro-oncology trial (PNOC022, clinicaltrials.gov identifiers: NCT05009992).

Positions

2019 – Present	PhD- candidate, Utrecht University, Utrecht, The Netherlands
2017 – Present	Clinical Trial Manager Neuro-Oncology, Princess Maxima Center, Utrecht, The Netherlands
2012 – 2017	Physiotherapist, FS Fysio, Cappelle aan den Ijssel, The Netherlands

Honors

2023	Finalist, Nationwide Network and Registry of Histopathology and Cytopathology (PALGA) award

Grants

Round III grant funding by the DIPG DMG Research Funding Alliance (DDRFA) to study the gut microbiome in the PNOC022 trial ($94,241)

GEOGRAPHICAL SURVIVAL COMPARISON AND ESTIMATED LONG TERM SURVIVAL OUTCOMES OF PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS FROM 31 EUROPEAN COUNTRIES – RESULTS FROM THE POPULATION BASED EUROCARE PROJECT

Raoull Hoogendijk[1], Riccardo Capocaccia[2], Jasper van der Lugt[1], Mariëtte E.G. Kranendonk[1], Eelco W. Hoving[1,3] Pieter Wesseling[1,4] Otto Visser[5], Dannis G. van Vuurden[1], Gemma Gatta[6], Henrike Karim-Kos[1,5] and the EUROCARE Working Group

1 Princess Máxima Center for Pediatric Oncology, Utrecht, The Netherlands
2 Editorial Board, Epidemiol Prev, Milan, Italy
3 Department of Neurosurgery, University Medical Center Utrecht, Utrecht, The Netherlands
4 Department of Pathology, Amsterdam University Medical Centers, Amsterdam, The Netherlands.
5 Department of Research and Development, Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands
6 Evaluative Epidemiology Unit, Department of Epidemiology and Data Science, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy,

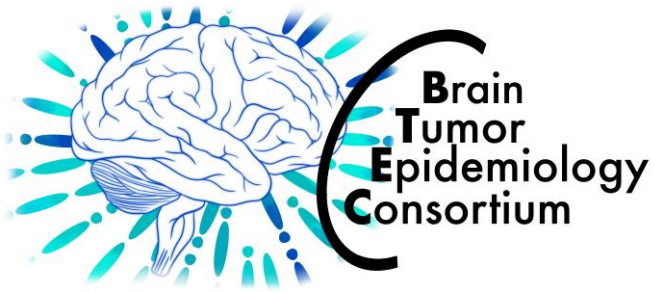
Background:
Survival outcomes of pediatric central nervous system (CNS) tumors have been reported to vary largely across countries in Europe. Additionally, up-to-date long-term survival outcomes have not been reported for clinically relevant groups of pediatric CNS tumors. Understanding the geographical variations and long-term survival outcomes can provide valuable information for healthcare policymakers and clinicians, aiding in the formulation of effective healthcare policies and strategic clinical planning. This EUROCARE study is the first to report these outcomes for clinically relevant groups of pediatric CNS tumors.

Materials and Methods:
Survival of 14,689 children (<15 years) diagnosed with a CNS tumor between 2008 and 2013 from 31 European countries was compared for the period 2008-2013 using cox regression models. A multivariate model, including the proportion of non-malignant CNS tumors, and age at diagnosis was used to compare adjusted risks of dying from a CNS tumor between countries using Germany as reference. Additionally, we analyzed data on 15,242 children (<15 years) diagnosed with a CNS tumor between 1998-2013 from 31 European countries with follow-up until 31/12/2014 to estimate up-to-date 15-year observed survival (OS) for the period 2010-2013 assuming that the risk of death was constant over time.

Results:
Five-year observed survival (OS) of low-grade gliomas (LGGs) for most countries was >90%. Three countries with comparable hazard ratios (2.6-2.7) showed to have a significantly higher risk of dying compared to Germany. Large variation in survival was seen for high-grade gliomas (HGGs); 0%-70%. When analyzing HGGs, six countries had a significantly higher risk of dying with hazard ratios ranging from 1.2 to 4.2. When excluding malignant gliomas, NOS (ICD-O-M9380/3) from the HGGs the risk of dying became comparable for two out of the six countries. For HGGs, only one country had a significant

lower risk of dying. For Medulloblastomas, 5-year OS within the majority of countries ranged between 40-70% but with some countries having no patients surviving their disease. Seven countries had significantly worse survival outcomes with hazard ratios ranging from 1.7-3.2. No countries were found to have better survival outcomes.
As a result of the high long-term mortality rate of 16 per 1000 surviving patients per year, ependymomas had an estimated 15-year OS of 62%. For diffuse astrocytomas estimated 15-year OS was 74%. Long-term mortality for surviving glioblastoma patients was null resulting in a projected 15-year OS of 20%. For medulloblastomas 15-year OS is estimated at 56%. AT/RTs including PNETs and with high-grade gliomas (HGGs) had an estimated 15-year OS of 28% and 19% respectively.

Conclusions:
This population-based study provides an insightful comparison of survival from CNS tumors in children between European countries corrected for potential incompleteness of non-malignant CNS tumors and misclassification of NOS tumors. Survival disparities were still seen for all tumor groups. Additionally, we are the first to estimate long term survival outcomes for clinically relevant groups of pediatric CNS tumors. These results will enhance patient-centered care, and contribute to the overall improvement of healthcare systems.



BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

Submitted Abstracts

(in order of presentation in the program)

Survival patterns of paediatric central nervous system tumours in Germany 1980-2016: a nationwide assessment based on data from the German Childhood Cancer Registry

Maike Wellbrock, Mathias Voigt, Cecile Ronckers, Desiree Grabow, Claudia Spix, Arndt Borkhardt, Daniel Wollschläger, Friederike Erdmann

Background: Tumours of the central nervous system (CNS) represent the most frequent solid tumours in children, accounting for roughly 25% of all cancers in children between the ages 0 and 14 in most of Europe. CNS tumours comprise a heterogeneous group of entities with substantial differences in biology, incidence pattern, histology, therapy and prognosis. Since primary preventive measures are lacking, improving survival probabilities and long-term well-being remain primary goals. With this report, we provide the first long-term assessment of time trends in survival patterns for paediatric CNS tumours in Germany.

Materials and Methods: Using data from the German Childhood Cancer Registry (GCCR), we analysed all children diagnosed with a CNS tumour at ages 0-14 years in 1980-2016. We calculated five-year overall survival (OS) estimates and assessed temporal survival patterns by tumour type, sex, age at diagnosis and tumour behaviour. Moreover, we calculated average annual percentage changes (AAPC) with corresponding 95% confidence intervals (CI) of the respective five-year OS estimates for malignant and non-malignant CNS tumours for the diagnostic period 1991 to 2016.

Results: The five-year OS from CNS tumours (all subtypes combined) improved from 63% in the 1980s, 70% in the 1990s to 79% in 2010-2016 (AAPC=0.63% (95% CI: 0.47; 0.79) for 1991-2016). These improvements have occurred across all age groups and virtually all tumour types, whereas temporal patterns varied to some extent by tumour type. We observed exceptional improvements for children diagnosed at ages 1-4 years and for those diagnosed with ependymomas and choroid plexus tumours (from 54% in the 1980s to recently 81%). While the survival improvements in ependymomas and choroid plexus tumours have levelled-off at around 80% since the Millennium, survival improvements for astrocytomas were evident over the entire period, reaching 84.4% in 2010-2016. For the subgroup of “Other gliomas”, five-year survival remained comparatively low over time (59.4% in the 1980s and 56.3% in 2010-2016).

Conclusions: Five-year survival probabilities improved substantially across all age groups and virtually all tumour types. Implementing nationwide standardised treatment protocols, which particularly focused on treatment stratification, has certainly contributed to the observed survival improvements. These remarkable enhancements have led to a steadily growing population of CNS tumour survivors with diverse health biographies and risk of lifelong adverse impact on health and wellbeing. Nonetheless, as survival for some paediatric CNS tumour types remains comparatively low, further research addressing both clinical factors and socioeconomic background is warranted.

Epidemiology, clinical data and long-term functional outcomes for operated central neurocytoma patients: preliminary results of the French experience

L. Bauchet[*1,2,3,] C-H. Mallereau[*4], G. Virbel[*5], F. Severac[6], M; Bilger[4], S. Zouaoui[1], A. Darlix[2,3,7], F Bauchet[3], J. Pallud[8], E. Lefevre[9], P. Roblot[10], M. Peyre[9], J. Nicolau[11], L. Klotz[11], Y. Sahler[12], T. Levan[13], I. Mezjan[14], A. Choucha[15], M. Rivollier[16], C. Bouloud[17], P. Page[18], T. Picard[19], T. Metayer[20], A. Gavotto[21], A. Sellier[22], L. Terrier[23], J. Claquin[24], J. Todeschi[4], H. Cebula[4], S. Chibbaro[4], V. Rigau[25], B. Trétarre[26], B. Lhermitte[27], F. Proust[4], G. Noel[5],

With the participation of the Club de Neuro-Oncologie de la Société Française de Neurochirurgie (CNO-SFNC) and The French Brain Tumor DataBase (FBTDB)

1. Department of Neurosurgery, CHU, 2. IGF, University of Montpellier, CNRS, INSERM, 3. French Brain Tumor DataBase, Registre des Tumeurs de l'Hérault, ICM, Montpellier; 4. Department of Neurosurgery, CHU, 5. Department of Radiation Oncology, Institut de Cancérologie (ICANS), 6. Department of Epidemiology, CHU, Strasbourg; 7. Medical Oncology Department, ICM, Montpellier; 8. Department of Neurosurgery, Hopital Sainte Anne, 9. Department of Neurosurgery, Hôpital de la Pitié-Salpétrière, APHP, Paris; 10. Department of Neurosurgery, CHU Pellegrin, Bordeaux; 11. Department of Neurosurgery, CHU, Toulouse; 12. Department of Neurosurgery, CHU, Rennes; 13. Department of Neurosurgery, CHU, Dijon; 14. Department of Neurosurgery, CHU, Nancy; 15. Department of Neurosurgery, Hopital de la Timone, Marseille; 16. Department of Neurosurgery, CHU, Reins; 17. Department of Neurosurgery, Fondation Rothschild, Paris, 18. Department of Neurosurgery, CHU, Poitiers; 19. Department of Neurosurgery, HCL, Lyon; 20. Department of Neurosurgery, CHU, Caen; 21. Department of Neurosurgery, CHU, Nice; 22. Department of Neurosurgery, hopital militaire, Toulon; 23. Department of Neurosurgery, CHU, Rouen; 24. Department of Neurosurgery, CHU, Nantes; 25. Department of Pathology, CHU, 26. Department of Epidemiology, Registre des Tumeurs de l'Hérault, ICM, Montpellier; 27. Department of Pathology, CHU, Strasbourg, France.

Background: Central neurocytoma (CN) is a rare primary brain tumor (WHO grade 2) for which there are very few epidemiological data and even fewer studies regarding patient outcomes. In this presentation, we provide epidemiology and clinical data as well as report long-term outcomes for operated CN patients.

Materials and Methods: Firstly, we collected data from the "French Brain Tumor DataBase" (FBTDB) cases and analyzed the incidence, sex-ratio, median age of all newly diagnosed and histologically confirmed CN, in France, between 2006 and 2015. Secondly, clinical, pathological and therapeutic records of adult patients were retrospectively reviewed to extract the relevant clinical factors for cases with sufficient information at 41 French centers. Thirdly we performed a cross-sectional quality of life study in daily practice for 65 CN patients.

Preliminary results: Between 2006 and 2015, 214 incident cases of newly diagnosed and histologically confirmed CN were recorded. The number of male/female was 106/108 and median age at diagnosis was 31 years (15 cases <18 years and 4 cases >70 years old). The crude rate was 0.034 per 100,000 persons per year.

Among 114 CN patients with sufficient information, the main clinical signs at presentation were intracranial hypertension [headache (86.7%), nausea/vomiting (36.7%), papilledema (34.7%), psychomotor slowing (23.2%), altered alertness (14.2%)]. The CN location was in one of the two lateral ventricles, in the third ventricle, or involved in multiple ventricles in 60%, 9%, 31% of cases, respectively. Median and mean initial tumor volumes

were 32.5 and 42.3 cm^3. A ventricular dilatation was present in 73/107 cases. Resection was performed in 108 patients (total, subtotal (>80%) and partial resection in 38/54/16 cases respectively). Postoperative mortality included three patients (2.6%). Immediate postoperative motor deterioration occurred in 49/112 (43.7%) patients. One month postoperatively, 51/107 patients (47.7%) suffered from cognitive impairments (memory disturbances) of varying intensity. Pre/or per/or post/operative external ventricular draining was performed in more than 50% of patients. Finally, a definitive ventricular-peritoneal/atrial-shunt was placed in 35/105 patients. Seventeen patients received radiation therapy during their management. Six patients received adjuvant radiotherapy and 11 patients underwent radiotherapy for local failure. Among these 11 patients, 6 were irradiated after a new resection and 5 patients without new surgery. Five-year PFS and 5-year OS were 78.6% (88/112 patients) and 93.0% (106/114 patients), respectively.

Sixty-five survival patients completed self-questionnaires (EORTC QLQ C30 and BN20, and specific outcome questionnaires). The analysis of the EORTC QLQ C30 and BN20 questionnaires is ongoing. Regarding functional outcomes, 41 patients (63.1%) returned to professional activity, 47 patients (72.3%) resumed driving, 22 patients (33.8%) required daily treatment for chronic epilepsy and 51 patients (78.4%) kept a “good” performance status (defined as KPS > 70) at time of interview.

Conclusions: CN mainly affects young adults and its oncological prognosis is quite favorable, but long-term disabilities must be taken into account. The analysis of long-term quality of life appears fundamental in order to define the best therapeutic strategies.

Standard of care for follow up for neurovascular late effects after radiotherapy for paediatric brain tumours.

[1]Louise Tram Henriksen, [2]Laura Toussaint, [3]Karen Van Beek, [4]Stéphanie Bolle, [5]Charlotte Demoor-Goldschmidt, [6]Jenny Gains, [7]Morten Høyer, [8]Sofie Isebaert, [9]Geert Janssens, [10]Rolf-Dieter Kortmann, [11]Catia Martins Pedro, [12]Beate Timmermann, [13]Katrin Scheinemann, [7]Yasmin Lassen-Ramshad

[1] Centre for Paediatric and Adolescent Cancer, Department of Paediatric and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark

[2] Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark; Aarhus University, Department of Clinical Medicine, Aarhus, Denmark

[3] Department of Radiation Oncology, UZ Leuven & Department of Oncology, KU Leuven, Leuven 3000, Belgium

[4] Institut Curie, Department of Radiation Oncology & Proton Centre, Paris, France; Institut Gustave Roussy, Department of Radiation Oncology, Villejuif, France

[5] Cancer and Radiation Team, INSERM UMRS 1018, Villejuif, France & Paediatric oncology and hematology, university hospital of Caen, Caen, France & Paediatric oncology and hematology, university hospital of Angers, Angers, France

[6] Department of Oncology, University College London Hospitals NHS Foundation Trust, London NW1 2PG, UK

[7] Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark

[8] Department of Radiation Oncology, University Hospitals Leuven, Leuven, Belgium

[9] Department of Radiation Oncology, University Medical Center Utrecht, and Princess Maxima Center for Pediatric Oncology, The Netherlands

[10] West German Proton Therapy Centre (WPE), Essen University Hospital, Essen, Germany

[11] Radiotherapy Department, Instituto Português de Oncologia Francisco Gentil, Centro de Lisboa, Lisbon, Portugal

[12] West German Proton Therapy Centre Essen (WPE), Essen University Hospital, Essen, Germany; Department of Particle Therapy, University Hospital Essen, Essen, Germany;West German Cancer Centre (WTZ), German Cancer Consortium (DKTK), Essen, Germany

[13] Division of Oncology/ Hematology, Children's Hospital of Eastern Switzerland, St. Gallen, Switzerland; Faculty of Health Sciences and Medicine, University of Lucerne, Lucerne, Switzerland

Background: Long-term survivors of paediatric brain tumours are at an increased risk of developing neurovascular large or small vessel disease. Radiation therapy has been proposed as risk factor. This study aimed at mapping the current European standard of care of follow up for neurovascular toxicity following radiotherapy in childhood.

Materials and Methods: A web-based survey, prepared in the frame of the HARMONIC study (harmonicproject.eu) together with the SIOPE Radiotherapy Working Group, was distributed to members of PANCARE and the SIOPE Brain Tumour Group. The survey assessed follow up for neurovascular disease following radiotherapy in childhood for a brain or skull base tumour. We report here the current screening practices.

Results: 33 participants from 15 different European countries completed the survey. 24 of the respondents (73%) reported not having specific guidelines for follow-up regarding neurovascular late effects after radiotherapy for a childhood brain or skull base tumour.
15/33 respondents (45%) screened routinely for neurovascular disease mainly with specific MRI sequences and regular blood pressure monitoring. 10/33 respondents (30%) also performed blood tests as part of the screening. The time interval for screening was individualized to the primary disease, radiation field or comorbidities. Six of 33 respondents (18%) performed lifelong screening and 10/33 (27%) screened for more than 10 years.
13/33 respondents (39%) only performed MRIs with specific neurovascular sequences if patients presented with symptoms suspicious for neurovascular disease and 11/33 (33%) if patients presented with new neurological symptoms.

Conclusions: Neurovascular screening after radiotherapy for paediatric brain tumours was performed in less than 50% of the responding institutions. Only few institutions have guidelines regarding neurovascular follow up. There is therefore a need for elaboration and harmonisation regarding follow up recommendations for this late effect.

The Epidemiology of CNS Tumors in Arab Countries: A Globocan Database Analysis

Sarah Al Sharie1, Abdallah Al-Ani2, Asem Mansour3, Maysa Al-Hussaini4*
1 Faculty of Medicine, Yarmouk University, Irbid, Jordan 2 Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman Jordan 3 Department of Pathology and Laboratory Medicine, King Hussein Cancer Center, Amman, Jordan 4 Department of Radiology, King Hussein Cancer Center, Amman, Jordan. *Correspondence to Dr. Maysa Al-Hussaini: mhussaini@khcc.jo

Background: Tumors of the Central Nervous System (CNS) pose a significant health concern worldwide, exhibiting varying incidence and patterns in different regions. This research is centered on the Arab world, which includes 22 countries, aiming to offer an in-depth analysis of the incidence, prevalence, and mortality rates of CNS tumors in these nations. The study considers the influence of genetic, environmental, and healthcare-related factors on these statistics.

Materials and Methods: Data from the Global Cancer Observatory was employed in our study to analyze the incidence, mortality, prevalence rates, and mortality to incidence ratios (IMR) of CNS tumors across 22 Arab countries, contrasting these figures with global data. The dataset encompassed information on new cases, deaths, and 5-year prevalence rates, segmented by country, age groups (0-14, 15-49, ≥50 years), and gender. We conducted descriptive statistics and comparative analyses to better understand these trends.

Results: In 2020, the Arab region, with its population of 449,228,296, contributed to 4.6% of the world's CNS tumor cases (14,177 new cases) and 4.72% of related deaths (11,860). Notably, males had a higher incidence of these tumors across all age groups, particularly in the 15-49 age bracket, which represented 8.97% of the global cases in this category. The group aged 50 and above recorded the most new cases, suggesting an increased risk with advancing age. The incidence rates for both genders in the Arab countries were higher than the global average, especially in the 0-14 age group (8.77% for males and 8.97% for females). The mortality trends were in line with the incidence rates, with the highest number of deaths observed in males over 50, and significant early-age mortality in the 0-14 age group (8.02% for males and 8.61% for females). The 5-year prevalence of CNS tumors in the Arab countries totaled 35,382 cases, with the most prevalent being in the ≥50 age group (7.92% for males and 8.12% for females). Egypt recorded the highest figures for new cases (4,499) and deaths (1,170). The incidence-to-mortality ratio in the Arab countries was marginally lower than the global average, showing variations across different countries and genders.

Conclusions: The findings of our study highlight the substantial impact of CNS tumors in the Arab world, marked by noticeable differences in incidence and mortality rates across various age groups and between genders. This underscores the urgency for improved healthcare approaches and increased resources dedicated to tackling the challenges associated with CNS tumors in these countries.

International Benchmarking of Childhood Cancer Survival by Stage (BENCHISTA Project): Results for medulloblastoma

Authors: Botta L, Didonè F, Bailey S, Lopez-Cortes A, Pritchard-Jones K, Gatta G and the BENCHISTA Project Working Group.

Background: The BENCHISTA Project aims to better understand the factors contributing to geographical differences in overall survival (OS) for childhood cancer (CC). Its main hypothesis is to assess how variations in the stage at diagnosis might affect these outcomes. The project collaborates with population-based cancer registries (PBCRs) and applies the internationally recognized Toronto Staging Guidelines (TG) to six types of childhood solid tumours, including medulloblastoma.

Materials and Methods: PBCRs collected data items according to the TG on all incident cases of medulloblastoma across 24 EU countries as well as Australia, Brazil, Canada, and Japan. The study included children aged 0-14yrs diagnosed over a consecutive three-year period spanning from 2013-2017. A minimum follow-up period of three years was conducted. PBCRs submitted depersonalized patient-level datasets incorporating Toronto Tier 1 or Tier 2 staging information based on available clinical support and/or legal access to clinical records. Three-year OS by stage was analysed using standard Kaplan-Meier methods. Multivariate analysis utilized a Cox model adjusted for age, stage, and geographical region. PBCRs optionally submitted additional patient-level data, including details on staging investigations, treatment modalities, and non-stage prognostic factors (molecular classification as WNT or SHH subtype) specific to medulloblastoma.

Results: Sixty-nine PBCRs contributed data on 1,518 cases of newly diagnosed medulloblastoma among children aged 0-14yrs during the period 2014-2017. Among these, 34% occurred in children aged 0-4yrs. Toronto stage distribution (Tier 2) was M0 (58%), M1 (6%), M2 (7%), M3 (18%) and M4 (0%), with 11% cases unable to be staged using information available to the PBCRs. Of the 1,074 cases with staging investigation information collected at patient-level by PBCRs, CSF cytology was performed/not performed/unknown in 73%, 9% and 18% respectively. Whole neuroaxis MRI scan was performed/not performed/unknown in 86%, 4% and 10%, respectively. The probability of having any M 1-4 stage at diagnosis compared to Central Europe was significantly higher in the UK and Ireland (OR=1.45).

Approximately 30% of cases included data on molecular subtype testing for WNT and SHH. Among the 445 cases with testing performed, the result was positive for 12% and 21% respectively. Information regarding treatment modalities was available for 1,228 cases at patient-level. Notably, 21% of these cases were documented as only receiving surgery and chemotherapy but no radiotherapy. For those not receiving radiotherapy, 77% was under 5yrs, and 56% under 3yrs of age.

Three-year OS for the entire cohort was M0:85%, M1:74%, M2:80% and M3:64%. Across different regions, three-year OS varied between 82% (Central Europe) and 73% (Eastern Europe). European Eastern countries faced the highest risk of mortality, despite no apparent differences in stage distribution compared to other European regions.

Conclusions: The BENCHISTA Project has demonstrated that PBCRs can access information on the international consensus TG to assign tumour stage for most cases of medulloblastoma at a population-level. However, access to molecular variables remains less comprehensive (~30%). Nonetheless, prevalence of molecular subtypes aligns with findings from clinical trials. The widespread adoption of TGs should streamline international comparisons and aid in identifying factors crucial for improving CC outcomes and reduce inequalities.

Impact of Maternal Health and Demographics on Childhood Brain Tumor Incidence: An Epidemiological Study

Julia Botvinov1, Syed A. Sarwar2, Geoffrey R. O'Malley, Jr.1, David Adams1, Shreyes Manivel1, Nicholas D. Cassimatis1; Jasdeep S. Hundal, PsyD3; Nitesh V. Patel, MD2

1Department of Neurosurgery, Hackensack Meridian School of Medicine, Nutley, NJ, USA. 2Department of Neurosurgery, HMH-Jersey Shore University Medical Center, Neptune, NJ, USA. 3Department of Neuropsychology, HMH-Jersey Shore University Medical Center

Background: Childhood brain tumors (CBT) represent the second most common form of childhood malignancy. Maternal health factors and demographics have long been subjects of epidemiological studies as they are thought to influence the intrauterine environment and thus may contribute to the developmental origins of various childhood diseases, including cancers. In the present study, we aim to assess whether maternal delivery and demographic factors are correlated with CBT incidence in New Jersey (NJ).

Materials and Methods: We retrospectively analyzed pediatric brain tumor incidence rates in NJ with average household income, different birth delivery methods, gender, and age groups. Delivery, gender, and age data was sourced from New Jersey State Health Assessment Data. Income data was sourced from the American Community Survey.

Results: A nonsignificant correlation between CBT incidence and average income was observed (r=0.166, *p*=0.471). The Cesarean Delivery Rate (-0.067, *p*=0.773), Low-Risk Cesarean Delivery Rate (r=-0.215, *p*=0.350), Primary Cesarean Delivery Rate (r=-0.220, *p*=0.338), Vaginal Birth After Cesarean Section Delivery Rate (r=0.379, *p*=0.090), and Percentage of Preterm Births (<37 weeks) (r=0.066, *p*=0.778) all demonstrated nonsignificant correlations with CBTs. There were no observed differences between male and female children for CBT incidence (t=0.6658, *p*=0.5243). The CBT incidence rates were 3.80 for ages<1, 4.30 for 1-4, 3.70 for 5-9, 3.05 for 10-14, and 2.55 for 15-19. The ANOVA found no statistically significant differences among these age groups (F=4.14, *p*=0.076).

Conclusions: The analysis did not find significant correlations between pediatric brain tumor incidence rates and the investigated maternal or demographic parameters. These findings suggest that these specific factors may not play a predominant role in influencing pediatric brain tumor occurrences**.**

Brain tumor classification by enzymatic DNA methylation sequencing of cell free DNA from cerebrospinal fluid

Aaron Michael Taylor 1, Jody T. Lombardi 1, Areeba Patel 2, Jonathan Martin3, Markus J. Bookland3, David S. Hersh3, Evan Cantor3, Xianyuan Song4, Felix Sahm 2, Patrick Kwok-Shing Ng 1,5, Joanna J. Gell 1,3,5, Ching C. Lau 1,3,5

1 The Jackson Laboratory for Genomic Medicine, Farmington, Connecticut, USA; 2 German Cancer Research Center (DKFZ), Heidelberg, Germany ; 3 Connecticut Children's Medical Center, Hartford, Connecticut, USA; 4 Hartford Hospital, Hartford, Connecticut, USA; 5 University of Connecticut School of Medicine, Farmington, Connecticut, USA

Background - Array-based DNA methylation profiling is the gold standard for molecular classification of brain tumors. However, it relies on significant amount of input DNA extracted from surgical tissue, thus limiting its use for tumors where biopsy is challenging or limited in quantity. Cell-free tumor DNA (cfDNA) in cerebrospinal fluid (CSF) presents alternative opportunities for brain tumor diagnosis and disease monitoring following treatment. Novel enzymatic DNA methylation sequencing (EM-seq) methods may allow us to overcome input DNA limitations and accurately quantify methylation from cfDNA.

Methods - We performed methylation sequencing using the NEBNext EM-seq kit on cfDNA from archival CSF samples collected from three brain tumor patients with confirmed histopathological diagnoses. Variable amounts of input cfDNA (0.1ng-10ng) were tested. We utilized the *methylseq* pipeline for data processing. For tumor classification, data was limited to CpG sites overlapping with the MethylationEPIC array before analysis using MNP-Flex, a modified platform-agnostic version of the Heidelberg methylation classifier

Results - Using the EM-seq method, genomic coverage for 10 and 1ng input DNA samples (average: 46x and 26x, respectively) was sufficient for generating global All methylation profiles. Samples with 0.1ng input showed an average coverage of only 5.32x due to high levels of read duplication. However, methylation levels for CpG sites with at least 5x coverage were highly correlated across varying input DNA amounts, suggesting that lower input cfDNA could still be used for tumor classification based on relevant CpG sites. All three samples were classified correctly by CSF as compared with the matched tissue sample.

Conclusions - Using the MNP-Flex classifier, which was originally trained with methylation array data from tumor tissue, we successfully predicted brain tumor types (both high-grade glioma and medulloblastoma) with cfDNA methylation data down to only 0.1ng of input cfDNA, matching diagnosis based on tissue methylation and histopathology in this pilot study. Further classification of additional tumor types using CSF cfDNA is required to confirm the clinical utility of this platform for all tumor types.

Enrichment of a neutrophil-like monocyte transcriptional state in glioblastoma myeloid suppressor cells

J.K. Wiencke*, Emily Nissen*, Devin C. Koestler, Stan J. Tamaki, Courtney M. Tamaki, Helen M. Hansen, Gayathri Warrier, Sara Hadad, Lucie McCoy, Terri Rice, Jennifer Clarke, Jennie W Taylor, Lucas A. Salas, Brock C. Christensen, Karl T. Kelsey, Rondi Butler, Annette M. Molinaro. *co-first authors; these authors contributed equally

Background: Glioblastomas (GBM) are lethal central nervous system cancers associated with tumor and systemic immunosuppression. Heterogeneous monocyte myeloid-derived suppressor cells (M-MDSC) are implicated in the altered immune response in GBM, but M-MDSC ontogeny and definitive phenotypic markers are unknown.

Materials and Methods: Here we take an integrative approach of different RNA-seq data sets. First, signature gene sets of monocytic phagocyte populations, derived from published scRNA-seq studies, were compared to our bulk RNA-seq from isolated M-MDSCs and monocytes from GBM subjects using a gene set enrichment analysis (GSEA). The GSEA identified a common set of genes to M-MDSCs across all data sets that was reminiscent of neutrophil-like monocytes (NeuMo). Then, the presence of a NeuMo signature in M-MDSCs was validated using a semi-supervised nonnegative matrix factorization based approach to deconvolute the proportions of Neu-like and DC-like monocytes in these cells. Finally, scRNA-seq from isolated M-MDSCs and PBMC samples from GBM subjects was analysed and revealed new gene sets that were mapped back Neu- and DC-like states.

Results: With these approaches, we revealed heterogeneity in blood M-MDSC from GBM subjects and an enrichment in a transcriptional state reminiscent of neutrophil-like monocytes (NeuMo), a newly described pathway of monopoiesis in mice. NeuMo populations were also observed in M-MDSCs from lung and head and neck cancer subjects. Dexamethasone (DEX) and prednisone exposures increased the usage of Neu-like states, which were inversely associated with tumor purity and survival in isocitrate dehydrogenase wildtype (IDH WT) gliomas. Using an independent scRNA-seq dataset we confirmed the enrichment of Neu-like states in M-MDSCs from GBM subjects.

Conclusions: Collectively, these findings provide a framework for understanding the heterogeneity of M-MDSCs in GBM as cells with different clonal histories and may reshape approaches to study and therapeutically target these cells.

Establishing a "Medical Home" for Children with Incidental Brain Lesions

Kelsey M. Knight, MSN, APRN, CPNP-PC, MLS; Riley Hospital for Children, Indianapolis, IN; Scott L. Coven, DO, MPH; Riley Hospital for Children at IU Health, Division of Pediatric Hematology/Oncology/Stem Cell Transplant and Indiana University School of Medicine, Indianapolis, IN

Background: Incidental brain lesions are defined as asymptomatic lesions, with most of these lesions in pediatric patients demonstrating the radiologic appearance of a low-grade glioma (LGG).[1] These incidental lesions are often identified in children undergoing routine brain imaging for other concerns.[2] Furthermore, there is a lack of consensus regarding the appropriate treatment approach for these children, which often includes surveillance imaging or surgery.

Objective: To develop a unique program offering for patients with incidental lesions (worked up for another reason) that are concerning for a brain or spinal cord lesion including low-grade glioma in the differential diagnosis.

Materials and Methods: Prior to the establishment of a dedicated clinic, patients with incidental lesions were often followed by various providers from Neurosurgery, Neuro-Oncology, or Neurology. We often heard from caregivers that they were overwhelmed being seen in an Oncology clinic without a formal oncologic diagnosis. Additionally, our goal was to develop an imaging cadence and longevity of imaging that is tailored to this distinct patient population. Lastly, we developed a survey to better understand the patient journey regarding an incidental lesion. Questions evaluated how families obtain information about an incidental lesion and what they tell family members about their child's diagnosis. Additionally, we asked questions about coordinated care amongst a neurosurgical and neuro-oncology provider, and whether they felt their needs were met in this dedicated space. Lastly, we evaluated caregiver distress through the GAD-7 (General Anxiety Disorder) instrument.

Results: In February 2022, our Pediatric Neuro-Oncology Comprehensive Program started a monthly clinic combining a nurse practitioner from Neurosurgery and a physician from Neuro-Oncology, with a school liaison often present in the clinic. In 2022, we had 41 visit encounters and in 2023 we had 57 visit encounters. From this initial starting point, we established a REDCap™ registry identifying 109 total patients with an incidental lesion that were previously followed by one of the services: Neurosurgery, Neuro-Oncology, or Neurology. Out of these 109 patients, only two patients (1.8%) have been referred for neurosurgical intervention due to a growing lesion on subsequent interval imaging.

24/36 caregivers (response rate of 67%) completed the clinic survey. All caregivers felt value in seeing neurosurgery and neuro-oncology providers together. All caregivers felt their concerns were addressed during the visit and their needs met. 21/23 (91%) caregivers liked having a dedicated clinic for their child. 19/23 caregivers (83%) recall a discussion regarding biopsy/surgery. 17/23 caregivers (74%) report comfort with surveillance imaging being the treatment approach. Median GAD-7 score was 4, indicating minimal anxiety.

Conclusions: We have successfully formed a dedicated clinic for patients with incidental brain lesions concerning for a low-grade glioma. Our registry will help us with our long-term goal to describe the clinical outcomes for children with incidental lesions, better understand how to develop the ideal imaging cadence, and when we can safely discharge patients from the clinic.

References:

1. Kozyrev, D.A.; Soleman, J.; Tsering, D.; Keating, R.F.; Hersh, D.S.; Boop, F.A.; Spennato, P.; Cinalli, G.; Tamburrini, G.; Thomale, U.-W.; et al. Pediatric Thalamic Incidentalomas: An International Retrospective Multicenter Study. *J. Neurosurg. Pediatr*. 2022, 29, 141–149.
2. Soleman, J.; Roth, J.; Ram, Z.; Yalon, M.; Constantini, S. Malignant Transformation of a Conservatively Managed Incidental Childhood Cerebral Mass Lesion: Controversy Regarding Management Paradigm. *Childs Nerv. Syst*. 2017, 33, 2169–2175.

Association between congenital anomalies and childhood brain tumors in 22 million live births

Authors: Thanh T. Hoang, Jeremy M. Schraw, Michael D. Taylor, Sharon E. Plon, Philip J. Lupo, Michael E. Scheurer, on behalf of the GOBACK study team.

Background: Aside from ionizing radiation and specific syndromes, risk factors of childhood brain tumors (CBTs) are not well known. While there is evidence that children with congenital anomalies have a higher risk of developing a brain tumor during childhood or adolescence, specific congenital anomaly and CBT co-occurrences are not well documented. The objective of this study is to better characterize the co-occurrences of specific congenital anomalies and histologies of CBTs.

Materials and Methods: We leveraged a population-based registry linkage of births, congenital anomalies, and cancer from nine states. Dates of birth and last follow-up varied by state, ranging between January 1, 1990 to December 31, 2018, for a total of 22,599,099 live births. CBT classification was based on the International Classification of Childhood Cancer for children diagnosed up to age 18 years. Unadjusted preliminary analyses were conducted using Cox regression for co-occurring congenital anomalies and CBTs with at least 5 children. We conducted analyses for astrocytoma, medulloblastoma, ependymoma, atypical teratoid/rhabdoid tumor (ATRT), and mixed and unspecified gliomas ("mixed gliomas").

Results: There were 6,297 diagnosed with any CBT, and 64 co-occurring congenital anomalies and CBTs were analyzed (26 with astrocytoma, 13 with medulloblastoma, 3 with ependymoma, 5 with ATRT, and 17 with mixed gliomas). Forty-four associations were statistically significant (FDR<0.05; 18 with astrocytoma, 9 with medulloblastoma, 0 with ependymoma, 5 with ATRT, and 12 with mixed gliomas). As expected, the strongest associations included astrocytoma and neurofibromatosis (HR: 422), mixed gliomas and neurofibromatosis (HR: 259), and astrocytoma and tuberous sclerosis (HR: 119). Restricting to CBTs diagnosed after age 1 year, hydrocephalus without spina bifida was associated with an increased risk of astrocytoma, ATRT, and mixed gliomas (HR range: 8.3-53.5).

Conclusions: We confirmed known congenital anomaly and CBT associations and identified novel co-occurrences, which may provide insights into the development of CBTs.

Sex Differences in Adverse Events Post Treatment in Glioblastoma

Mantas Dmukauskas1, Gino Cioffi1, Kristin A. Waite1, Andrew E. Sloan2, Corey Neff3, Mackenzie Price3, Quinn T. Ostrom3,4, Jill S. Barnholtz-Sloan1,5
1Trans Divisional Research Program, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 2Piedmont Health, Neuroscience Service Line and Piedmont Brain Tumor Center, 3Department of Neurosurgery, Duke University School of Medicine, 4The Preston Robert Tisch Brain Tumor Center, Duke University School of Medicine, 5Center for Biomedical Informatics and Information Technology, National Cancer Institute

Background: Glioblastoma (GB) is the most common type of glioma, with a median diagnosis age of 64 years. Despite aggressive multi-modal therapies, GB remains uniformly lethal. Males have worse survival rates compared to females. Standard of care (SOC) follows the Stupp protocol, studied in those <70 years, consisting of a combination of surgery, radiation, and Temozolomide. Currently treatment strategies, particularly in those ≥66, are based on physician and/or individual preference, considering prognostic survival benefits and potential toxicities and adverse event (AE) risk. Recent studies have suggested the presence of a sex-bias in AE development in individuals receiving cancer treatment. However, potential sex bias in AE development in individuals with GB undergoing various treatment modalities has not been examined. We identify sex differences in treatment patterns and AE in individuals ≥66 at GB diagnosis.

Materials and Methods: We utilized the Surveillance, Epidemiology and End Results Program-Medicare dataset to examine sex differences in treatment patterns and AEs in GB patients ≥66 years. We identified 12,165 individuals diagnosed with GB between 2004-2017. Sex differences were assessed based upon their treatment modality: no-treatment (NT), SOC (surgery + radiation + Temozolomide), or other treatment (OT) (any other combination of surgery, radiation and/or Temozolomide). AE categories were identified using the common terminology criteria of adverse event (CTCAE) designed to identify AEs in clinical trials. Multivariable logistic regression was used to determine the odds of experiencing an AE in males relative to females stratified by treatment group.

Results: In older individuals diagnosed with GB, males received SOC (20% vs 17%) and OT (59% vs 57%) more than females. Females received no GB-specific treatment (NT) more than males (26% vs 21%). In individuals who received SOC, the most reported AE were nervous system disorders (male/female 74%/76%) followed by vascular disorders (male/female 61%/65%). Overall, sex-differences in AE profiles were observed and were dependent upon treatment modality. In individuals who received SOC, females were more likely to have an AE in 7 CTCAE categories, compared to males who were more likely to have an AE in 4 categories. Females receiving SOC were more likely to develop gastrointestinal disorders (OR=0.76; 95% CI,0.64-0.91, p=0.002) or blood and lymphatic system disorders (OR=0.79; 95% CI,0.66-0.95, p=0.012). Males with GB receiving SOC were more likely to develop cardiac disorders (OR=1.21; 95% CI,1.02-1.44, p=0.029) and renal disorders (OR=1.65; 95% CI,1.37-2.01, p<0.001). Sex differences in gastrointestinal disorders were observed depending upon treatment modality. In females receiving surgery and radiation, females had higher odds of gastrointestinal disorders compared to males (OR=0.82; 95% CI,0.69-0.97, p=0.019). In contrast, males had higher odds when receiving surgery and Temozolomide (OR=1.49; 95% CI,1.12-2.00, p=0.007).

Conclusions: This study demonstrates that there are sex differences in treatment modalities received in individuals ≥66 years diagnosed with GB. Males were more likely to receive SOC compared to females. Additionally, sex difference in the development of AE were observed in GB treatment modalities. These results suggest that health care providers should consider how sex biases may impact AE development when providing GB treatment for elderly individuals.

Investigating Diagnostic Cost Disparities for Central Nervous System Tumours Across Canadian Provinces

Keyun Zhou, Yan Yuan, Emily Walker - University of Alberta, Alberta – Canada

Background: Primary central nervous system (CNS) tumors are a significant public health challenge, affecting millions of patients. Timely and accurate diagnosis is crucial for improving patient outcomes. Despite being publicly funded, differences in provincial policies, needs, infrastructure, and resource availability have resulted in variations in healthcare delivery across Canada. The cost-effectiveness of managing rare cancers like primary CNS tumors has received little attention. This study aims to investigate the diagnostic costs associated with CNS tumors in Canada and potential disparities in tumor management and resource allocation across regions.

Materials and Methods: Data were obtained from the Canadian Institute for Health Information, integrating information from the National Ambulatory Care Reporting System (outpatient) and the Discharge Abstract Database (inpatient). The study included patients diagnosed with CNS tumors in all provinces and territories from 2010-2014. Diagnostic costs were calculated for each patient as one-year pre-diagnostic cumulative costs. Quantile regression analysis was used for the 10th, 50th, and 90th percentiles to examine associations between diagnostic costs and various factors, including province, age group (0-14, 15-39, 40-64, 65+), sex (female/male), encounter type (inpatient/outpatient), and tumor site (brain, meninges, other nervous systems, pituitary and craniopharyngeal duct).

Results: A total of 24,671 CNS tumor patients were identified, with Alberta and Ontario accounting for 99% of outpatient cases. Therefore, the analysis was limited to 4,900 patients with malignant CNS tumors from these two provinces due to a high degree of missing data in other regions. Examination of cost percentiles revealed that the top 10% of patients (90th percentile) accounted for 46% of pre-diagnostic expenses, highlighting challenges in resource allocation. The median inpatient diagnostic cost was CAD $12.11K (10th-90th percentile: $CAD 5.29-35.71), and the outpatient diagnostic cost was CAD $1.04K (CAD $0.43-9.00). The pediatric (0-14) and senior (65+) age groups incurred the highest costs.

Significant cost differences were observed across Alberta and Ontario, particularly at the 10th and 90th percentiles in pediatric and senior age groups. Alberta had higher inpatient costs across all percentiles and tumor categories, with the largest disparities in the 0-14 age group. Outpatient costs did not differ significantly, except for the top 10% of cases in the 0-14 age group, where Alberta had higher costs.

Conclusions: This study provides insights into the differences in diagnostic costs for malignant CNS tumors between Alberta and Ontario, highlighting variations across provinces and age groups. The cost differences underscore the need for further investigation into the underlying factors contributing to these disparities. Such investigations can help identify strategies to reduce diagnostic costs in areas with higher expenditures and target specific subpopulations. However, the analysis was limited by missing data, emphasizing the need for improved data collection methods to understand potential variations across all Canadian regions. Efforts should be focused on improving data completeness and standardizing reporting practices across provinces to enhance the quality of information available for public health decision-making and policy development.

Parental occupational exposures and *de novo* neurocutaneous syndromes in the offspring: findings from a register-based Swedish case-control study.

Christina-Evmorfia Kampitsi, Marios Rossides, Hanna Mogensen, Mats Talbäck, Jenny Selander, Pernilla Wiebert, Ann Nordgren, Giorgio Tettamanti, Maria Feychting

Background: Neurocutaneous syndromes are associated with a wide range of long-term effects, including a particularly raised risk for childhood brain tumors. Yet, risk factors for their *de novo* occurrence are poorly understood. Currently, no studies are available on the potential effects of parental exposures, despite their teratogenic potential having been assessed in the context of somatic birth defects. To the best of our knowledge, therefore, this is the first study aiming to evaluate how parental occupational chemical exposures around conception affect the risk of *de novo* neurocutaneous syndromes, particularly neurofibromatosis type 1 (NF1) and tuberous sclerosis complex (TSC).

Materials and Methods: This population-based nested case-control study included children born in Sweden, 1960–2014. Cases were 2,792 individuals with *de novo* neurocutaneous syndromes identified through nationwide healthcare registers. They were matched to 139,600 population controls by birth year and sex. We assessed parental occupational chemical exposures using a job-exposure matrix, retrieving occupational information from administrative population registers. We estimated odds ratios (OR) and 95% confidence intervals (CI) of *de novo* neurocutaneous syndromes, NF1, and TSC through conditional logistic regression.

Results: Offspring of either parent occupationally exposed to solvents overall exhibited increased NF1 risk (ORmaternal=1.23;95% CI, 1.02–1.48; ORpaternal=1.13;95% CI, 1.01–1.27), driven by hydrocarbon solvents in both parents, and formaldehyde, trichloroethane, and toluene in fathers. There were indications for increased NF1 risk related to maternal occupational exposure to dusts overall, driven by quartz dust and stone and concrete; fathers had a single indication for wood dust. No associations with NF1 were observed for pesticides. For metals, an indication for iron exposure was the most notable among mothers, whereas an increased risk of NF1 related to paternal occupational exposure to metals overall (OR=1.16;95% CI, 1.02–1.31) was driven by chromium, iron, and nickel. Parental exposure to combustion particles overall was not associated with NF1 risk, although risk estimates were elevated for benzo(a)pyrene and polycyclic aromatic hydrocarbons. For TSC, risk estimates were generally around unity.

Conclusions: Occupational exposure to a range of chemical agents, especially in mothers, is associated with elevated risks of *de novo* NF1 but not TSC in the offspring. The distinctive high mutation rate of the NF1 gene may contribute to this divergence. If corroborated in subsequent studies, these findings could spearhead policies aimed at mitigating the impact of these modifiable risk factors on the occurrence of *de novo* NF1 and its ensuing outcomes, including childhood brain tumors.

Characteristics of Mental Health Disorder Among Central Nervous System Cancer and Other Childhood Cancer Patients – A Population-based Study for Medicaid Beneficiaries in Kentucky

Feitong Lei. PhD. Assistant Professor, Division of Cancer Biostatistics, University of Kentucky
Eric Durbin, DrPH, Assistant Professor, Division of Biomedical Informatics, University of Kentucky
Thomas Tucker, PhD, Professor, Department of Epidemiology and Environmental Health, University of Kentucky,
John Villano, MD, Division of Medical Oncology, University of Kentucky
*Bin Huang, DrPH, Professor, Division of Cancer Biostatistics, University of Kentucky

Background: The mental health of cancer patients is central for QOL and proper receipt of care. However, there's limited understanding of the prevalence of mental health disorders (MHD) and their follow up care among childhood central nervous system (CNS) cancer patients, particularly for underserved population such as Medicaid beneficiaries. This study is to explore the MHD prevalence for CNS and other childhood cancer diagnoses among Medicaid beneficiaries in Kentucky and examine utilization of mental health related (MHR) consultations.

Materials and Methods: The Kentucky Cancer Registry data were utilized to identify patients aged 19 or under with a first primary childhood cancer diagnosis during 2001-2017. Linking KCR data with Medicaid claims, we included patients with continuous Medicaid enrollment 12 months before and after their cancer diagnosis. MHD were identified using both International Classification of Diseases (ICD)-9 and ICD-10 codes. A descriptive analysis was conducted.

Results Among 898 childhood cancer cases identified from the registry data, 193 were CNS cases. Based on claims data 12 months prior to cancer diagnosis, 37% (n=71) of the CNS patients had a MHD compared to 31% (n=222) for the rest of childhood cancers. The rate increased to 59% (n=113) within 12 months post-diagnosis for CNS patients compared to 53% (n=376) for the rest of childhood cancers. More specifically, neuropsychiatric/ developmental disorders for CNS increased from 30% to 34%; mood disorder from 12% to 26%. For the rest of childhood cancer cases, the mood disorder has an even larger increase from 12% to 33%. 46% of CNS patients diagnosed with an MHD within a year post-cancer diagnosis utilized MHR consultations, compared to 34% for the rest of childhood cancer cases.

Conclusions: In the study, notable increases of MHD prevalences from pre-cancer diagnosis to post-cancer diagnosis were found among Medicaid-enrolled CNS and other childhood cancer patients in Kentucky. This increased prevalence post-diagnosis may result from the identification of pre-existing mental health conditions during cancer treatment, or the emergence of new mental health issues as a consequence of the cancer diagnosis and treatment. The low utilization of MHR consultation demonstrates the need for improved mental health access for childhood cancer patients.

Characterization of novel multi-target compounds for the treatment of glioblastoma

Aizpea Artetxe-Zurutuza, Joseba Elizazu, Nerea Iturrioz-Rodriguez, Jose Luis Marco, Ander Matheu

Background: Glioblastoma is characterized by a high heterogeneity at molecular and cellular level, which is associated with therapy resistance. In this context, the new idea "*one molecule-multiple targets*" for developing drugs to treat multifactorial diseases has been proposed and such compounds have been termed Multitarget Small Molecules (MSM). Indole is one of the most privileged scaffolds in chemistry, so it may serve as an effective probe for the development of new drugs against diseases, including cancer and glioblastoma.
In this project, we have generated three new families of compounds targeted against combining H3R/S1R modulation with AChE/BuChE, and MAO A/B inhibition in one MSM. Additionally,
the compounds present structural similarity with current HDAC inhibitors: Vorinostat (Family D), Belinostat (Family M) or Tubastatin A (Family F).

Materials and Methods: As an initial approach, MTT assays were performed to study the cytotoxicity of the compounds in U87 cell line, and the 6 most promising compounds were selected for their further characterization. The potential drugability of those compounds was predicted using online available tools *molinspiration* and *online BBB predictor*.
The inhibitory capacity of selected compounds on their potential targets was studied by western blot (HDAC inhibition), MAO inhibition assay (MAO inhibition) and Ellman's colorimetric method (ChE inhibition). In addition, the effect of these compounds on cell proliferation and apoptosis was studied by immunofluorescence assays.
Finally, RNAseq and proteomic studies were carried out for the most promising compounds, and DEG were validated in publicly available datasets.

Results: From all the initial compounds, D1, M1, M2, M3, F1 and F2 presented the most cytotoxic activity, and thus, were selected for their further characterization. Basing on their structure, the six compounds present good drugability, and are predicted to cross the blood-brain barrier.
All of them are able to inhibit HDACs activity, being the effect dose-dependent and related to their affinity to specific HDACs. Indeed, the inhibitory capacity of D1 and M3 was even higher than the compound of reference Vorinostat. Regarding MAO and ChE inhibition, D1, M3, F1 and F2 showed promising results, while M1 and M2 have lower or not inhibitory effect for MAO and ChE, respectively. In addition, selected compounds reduce cell proliferation and induce apoptosis in a dose-dependent manner, in patient-derived glioma stem cells and also in conventional glioblastoma cells.
Basing on these results, D1 and M3 were selected for RNAseq and proteomic studies. In both cases, DEG that were upregulated were related to cell cycle, while the downregulated ones are more associated with neurotransmission.

Conclusions: In this study, several novel compounds have been characterized that are able to reduce tumorigenic activity in patient derived glioblastoma stem cells both in functional and molecular level. Thus, these multi-target compounds are a novel and promising therapeutic strategy for the treatment of glioblastoma.

DESCRIPTIVE EPIDEMIOLOGY OF CHILDHOOD PRIMARY BRAIN TUMORS IN UGANDA; DATA FROM A TERTIARY CENTER

Victoria Mwebe Katasi[1], Michael E. Scheurer2,3, Ching Lau4, Roberta McKean-Cowdin5, Kimberly J. Johnson6

Mulago National Referral Hospital, Kampala, Uganda [1], Baylor College of Medicine, Department of Pediatrics, Houston, TX, USA2, Texas Children's Hospital Cancer Center Houston, TX, USA3, 4The Jackson Laboratory for Genomic Medicine in Farmington, CT, and Connecticut Children's Medical Center in Hartford, CT, USA, 5University of Southern California, Los Angeles, CA, USA, 6Brown School Master of Public Health Program, Washington University, St. Louis, MO, USA

BACKGROUND: Pediatric brain tumors are the second most common childhood malignancy and the most common solid tumor in children in high income countries. However, there is paucity of data from low- and middle-income countries (LMIC). Studies from high income countries (HIC) show 5-year survival rates of over 70%. However, the survival of children with brain tumors in LMIC is still poor with 1-year survival rates estimated to range between 40% to 66%. In Uganda, within the last 20 years, less than 10 studies about pediatric brain tumors have been published, with only two reporting patient survival. This underscores the need for more research in this area to drive improvement in care of these patients in Uganda.

STUDY OBJECTIVE: To determine factors affecting survival of children with primary brain tumors seen at Mulago National Referral Hospital (MNRH) from March 2019 to March 2023. Specifically, we determined median time to presentation, histological diagnosis for tumors diagnosed histologically, surgery, chemotherapy, and radiotherapy. We also estimated one-year survival.

METHODOLOGY: This was a retrospective, descriptive study conducted in the pediatric neuro-oncology clinic at MNRH that included patients seen in the clinic between March 2019 and March 2023. Initial date of symptom occurrence, date of presentation to a tertiary health center, date of surgery, date of histological diagnosis, radiotherapy start date, chemotherapy start date and vital status of the patient were used to calculate median times and one year survival. A tertiary health center was defined as one of the three hospitals where specialized neurosurgery and or neuro-oncology services were provided for the patients in this study (Mulago National referral Hospital, Mbarara Regional Referral Hospital and Cure International Children's Hospital). We also looked at the one-year survival of these patients. The data was analyzed using the R statistical package.

RESULTS: A total of 119 patients were diagnosed during this period and of these, the majority were male (55%). The age range of patients was 2 months to 17 years. The commonest presentation and diagnosis was headache (42%) and glioma (38%). Fifty-seven patients had surgical resection with a histological diagnosis. Thirty-five patients received radiotherapy. Thirty-four patients received chemotherapy. The median time to presentation from time of occurrence of initial symptoms was 141days. The median time to definitive surgery from time of presentation to a tertiary health center was 110.5 days. The median time to a histological diagnosis (except for DIPG, optic pathway gliomas and craniopharyngiomas who are still diagnosed using imaging and get no surgical excision) was 108 days. The median time to chemotherapy from time of diagnosis was 48 days. The median to radiotherapy from time to diagnosis was 179 days. The 1-year survival was 63% (95% CI 54% to 72%).

CONCLUSIONS

The survival of children with primary brain tumors in Uganda is comparable to that of some other LMIC and lower than in HIC. Delays in presentation for specialized care, in getting surgery and starting radiotherapy are some of the factors that may influence survival of these children.

Long-term antidepressant drugs use among Childhood CNS Tumor Survivors in Sweden: a register-based cohort study.

Javier Louro1, Hanna Mogensen1,2, Christina-Evmorfia Kampitsi1, Mats Talbäck1, Giorgio Tettamanti1, Maria Feychting1
1 Unit of Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
2 Department of Immunology, Genetics and Pathology, Cancer Precision Medicine, Uppsala University, Sweden

Background: While childhood central nervous system (CNS) tumors are relatively uncommon, they remain a significant health concern, with over 110 new cases diagnosed in Sweden every year. Therapeutic progress has notably improved survival rates, leading to a consistent rise in the population of childhood CNS tumor survivors. Previous studies have found a higher antidepressant usage in childhood cancer survivors, but it has not been studied specifically for childhood CNS tumor survivors even though depression, anxiety, and other mood disorders are more prevalent among this group. We aimed to analyze the long-term use of antidepressant drugs in childhood CNS tumor survivors.

Materials and Methods We performed a register-based cohort study nested in the Socioeconomic Consequences in Adult Life after Childhood Cancer (SALiCSS) research program, which included all childhood CNS tumor survivors diagnosed in Sweden from 2000 to 2015, with at least 5 years of follow-up after the cancer diagnosis. For each survivor, a control group of 5 individuals randomly selected from the general population and individually matched to cancer survivors by year of birth and sex was included for comparison. We fitted Cox proportional hazards regression models with age as timescale to estimate the hazard ratios (HR) with 95% confidence intervals (95%CI) of use of antidepressant drugs from the fifth year after diagnosis to the end of follow-up. Analyses were adjusted for sex, region of residence, and parental socioeconomic status (SES). A sensitivity analysis was also performed using the cancer survivors' siblings as a comparison group.

Results Our cohort included 1,011 childhood CNS tumor survivors and 4,934 matched controls. The mean age of diagnosis among cases was 10.63 years old. The risk of antidepressant use was significantly higher in childhood CNS tumor survivors compared with their matched individuals (HR = 1.34; 95%CI = 1.17-1.54). When stratifying by antidepressant type, the highest differences in risk were found in the use of non-selective monoamine reuptake inhibitors (HR = 2.03; 95%CI = 1.47-2.80). Similarly, when stratifying by cancer type, the highest risk of antidepressant use was found among survivors of astrocytoma and other gliomas compared with their matched comparisons (HR = 2.46; 95%CI = 1.55-3.90). Risk estimates were higher in males (HR = 1.61; 95%CI = 1.31-2.07) than in females (HR = 1.22; 95%CI = 1.02-1.45). When stratifying by parental SES, the raised risk estimates were seen only for survivors belonging to families with medium and high parental SES, but no differences were found among survivors in families with low parental SES. The sensitivity analysis was performed with 1,419 siblings and showed comparable results, demonstrating the robustness of our findings. These are preliminary analyses; SALiCCS data from Denmark and Finland will be included in the final analyses which will increase statistical power.

Conclusions Our results provide evidence that having a childhood CNS tumor is associated with an increased risk of long-term mental health problems. These results may allow a better understanding of the long-term effect of CNS tumors in survivors and highlight the need for further research in this field.

The effect of prior varicella zoster infection on a person's risk of glioma development.

Christine Ann Pittman Ballard, MPH[1]; Quinn T. Ostrom, PhD, MPH[2]; Glioma International Case-Control (GICC) Study Investigators, Christopher I. Amos[3], PhD; Melissa L. Bondy, PhD[4]; Kyle M. Walsh, PhD[2]

1 Gillings School of Global Public Health, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; 2 Department of Neurosurgery, Duke University School of Medicine, Durham, NC, USA; 3 Dan L. Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, TX, USA; 4 Department of Epidemiology and Population Health, Stanford University School of Medicine, Palo Alto, CA, USA.

Background: Many infectious agents have been studied in association with the development of glioma. However, the only infectious agent consistently associated with glioma risk is varicella zoster virus (VZV), which causes chickenpox at first infection (usually during childhood) and can be reactivated in later life as shingles. Although the biological mechanisms underlying this association remains incompletely characterized, history of VZV infection has been consistently inversely associated with glioma risk. Previous GWAS identified two independent risk alleles near the Epidermal Growth Factor Receptor (*EGFR*) gene. The EGFR protein has been observed to facilitate herpesvirus entry into human cells, and VZV can regulate *EGFR* activity through intricate feedback loops, suggesting potential biological interaction between *EGFR* polymorphisms and VZV infection in modulating glioma predisposition. We sought to investigate the effect of prior VZV infection on glioma risk in a case-control sample and investigate modification by *EGFR*.

Materials and Methods: Analyses included 4,574 glioma patients and 4,178 glioma-free controls from the Glioma International Case Control (GICC) Study. Participants completed a medical history questionnaire and underwent germline DNA profiling using the Illumina OncoArray. We excluded individuals that were from Baylor Medical College due to lack of controls. For this analysis we only examined cases that had a positive history of glioblastoma (GBM), and controls. 1833 cases of GBM and 1219 controls were included. Using multivariable logistic regression, we evaluated the effects of prior chickenpox or shingles on GBM risk, the effects of sentinel *EGFR* risk loci from prior GWAS (rs723527, rs75061358), and assessed whether VZV infection history modified SNP effects.

Results: 1126 cases (79.5%) and 1679 controls (82.9%) reported a positive history of chickenpox. Overall, a positive history of chickenpox was associated with lower odds of glioblastoma (mOR=0.84, 95% CI: 0.63, 1.11). Shingles was self-reported. Therefore, we only included a positive shingles infection if a person had a prior history of chickenpox. A prior history of shingles was reported by 13.1% of cases and 8.8% of controls (mOR= 1.15, 95% CI: 0.88, 1.50). *EGFR* variants rs75061358 and rs723527 were significantly associated with GBM risk (OR=1.32, 95% CI: 1.09, 1.61; and OR=1.18, 95% CI: 1.06, 1.34, respectively). We did not observe statistical interaction between either SNPs and personal history of chickenpox or shingles infections.

Conclusions: These results suggest that *EGFR* and VZV and both associated with GBM development. Further research is needed to determine the extent to which this relationship between VZV can act as a potential therapeutic target for glioma.

Maternal exposure to solvents from industrial sources during pregnancy and childhood cancer risk in California

Julia E. Heck, Stephanie Chen, Darcy van Deventer, Myles Cockburn

Background: Multiple solvents are established or suspected carcinogens in studies of adults, with adverse reproductive and child health endpoints additionally reported. A working group has identified industrial agents considered high priorities for evaluation by the IARC Monographs Program. Guided by these priorities, the study aimed to investigate the associations between childhood cancer and maternal exposure in pregnancy to three solvents: trichloroethane, tetrachloroethylene, and carbon disulfide.

Materials and Methods: The present study included 3188 central nervous system cancer cases (aged 0-19 years at diagnosis) identified from the California Cancer Registry and 283,141 controls randomly selected from California Birth Registry. We examined industrial releases of tetrachloroethylene and 1,1,1-trichloroethane within 3km of birth address, while we used a 5km buffer for carbon disulfide. We calculated the total exposure from all linked Toxic Release Inventory sites during each index pregnancy and assigned “ever/never” and “high/low exposed/unexposed” exposure, using median values. We utilized quadratic decay models to estimate cancer risks associated with maternal solvent exposure in pregnancy, with adjustment for birth year, maternal age, race and ethnicity, source of payment for prenatal care, residence in rural/urban area, census tract SES-index.

Results: Ever exposure to carbon disulfide might increase the risks of medulloblastoma (OR=1.85, 95% CI 1.01, 3.40) and ependymoma (OR=1.63, 95% CI 0.97, 2.74). There were no associations seen with tetrachloroethylene apart from a weak increase in all CNS tumors combined at the low level of exposure (OR=1.24, 95% CI 1.02, 1.51) whereas the high level of exposure was not associated (OR=0.95). 1,1,1-trichloroethane was not associated with any type of CNS tumor.

Conclusions: A number of studies have reported on central nervous system toxicity with carbon disulfide exposure. With regards to reproductive effects, carbon disulphide lowers sperm motility and has been linked with adverse birth outcomes including preterm birth, congenital malformations, emesis gravidarum, and pre-eclampsia. Our study is the first to suggest a relation between maternal carbon disulfide exposure and subtypes of CNS tumors.

Sex Differences in Adverse Events Post Treatment in Glioblastoma

Mantas Dmukauskas1, Gino Cioffi1, Kristin A. Waite1, Andrew E. Sloan2, Corey Neff3, Mackenzie Price3, Quinn T. Ostrom3,4, Jill S. Barnholtz-Sloan1,5
1Trans Divisional Research Program, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 2Piedmont Health, Neuroscience Service Line and Piedmont Brain Tumor Center, 3Department of Neurosurgery, Duke University School of Medicine, 4The Preston Robert Tisch Brain Tumor Center, Duke University School of Medicine, 5Center for Biomedical Informatics and Information Technology, National Cancer Institute

Background: Glioblastoma (GB) is the most common type of glioma, with a median diagnosis age of 64 years. Despite aggressive multi-modal therapies, GB remains uniformly lethal. Males have worse survival rates compared to females. Standard of care (SOC) follows the Stupp protocol, studied in those <70 years, consisting of a combination of surgery, radiation, and Temozolomide. Currently treatment strategies, particularly in those ≥66, are based on physician and/or individual preference, considering prognostic survival benefits and potential toxicities and adverse event (AE) risk. Recent studies have suggested the presence of a sex-bias in AE development in individuals receiving cancer treatment. However, potential sex bias in AE development in individuals with GB undergoing various treatment modalities has not been examined. We identify sex differences in treatment patterns and AE in individuals ≥66 at GB diagnosis.

Materials and Methods: We utilized the Surveillance, Epidemiology and End Results Program-Medicare dataset to examine sex differences in treatment patterns and AEs in GB patients ≥66 years. We identified 12,165 individuals diagnosed with GB between 2004-2017. Sex differences were assessed based upon their treatment modality: no-treatment (NT), SOC (surgery + radiation + Temozolomide), or other treatment (OT) (any other combination of surgery, radiation and/or Temozolomide). AE categories were identified using the common terminology criteria of adverse event (CTCAE) designed to identify AEs in clinical trials. Multivariable logistic regression was used to determine the odds of experiencing an AE in males relative to females stratified by treatment group.

Results: In older individuals diagnosed with GB, males received SOC (20% vs 17%) and OT (59% vs 57%) more than females. Females received no GB-specific treatment (NT) more than males (26% vs 21%). In individuals who received SOC, the most reported AE were nervous system disorders (male/female 74%/76%) followed by vascular disorders (male/female 61%/65%). Overall, sex-differences in AE profiles were observed and were dependent upon treatment modality. In individuals who received SOC, females were more likely to have an AE in 7 CTCAE categories, compared to males who were more likely to have an AE in 4 categories. Females receiving SOC were more likely to develop gastrointestinal disorders (OR=0.76; 95% CI,0.64-0.91, p=0.002) or blood and lymphatic system disorders (OR=0.79; 95% CI,0.66-0.95, p=0.012). Males with GB receiving SOC were more likely to develop cardiac disorders (OR=1.21; 95% CI,1.02-1.44, p=0.029) and renal disorders (OR=1.65; 95% CI,1.37-2.01, p<0.001). Sex differences in gastrointestinal disorders were observed depending upon treatment modality. In females receiving surgery and radiation, females had higher odds of gastrointestinal disorders compared to males (OR=0.82; 95% CI,0.69-0.97, p=0.019). In contrast, males had higher odds when receiving surgery and Temozolomide (OR=1.49; 95% CI,1.12-2.00, p=0.007).

Conclusions: This study demonstrates that there are sex differences in treatment modalities received in individuals ≥66 years diagnosed with GB. Males were more likely to receive SOC compared to females. Additionally, sex difference in the development of AE were observed in GB treatment modalities. These results suggest that health care providers should consider how sex biases may impact AE development when providing GB treatment for elderly individuals.

“De novo replication repair deficient glioblastoma, IDH-wildtype” is a distinct glioblastoma subtype in adults that may benefit from immune checkpoint blockade

Sara Hadad1, Rohit Gupta2, Nancy Ann Oberheim Bush1,3, Jennie W. Taylor1,3, Javier E. Villanueva-Meyer4, Jacob S. Young1, Jasper Wu2, Ajay Ravindranathan2, Yalan Zhang1, Gayathri Warrier1, Lucie McCoy1, Anny Shai1, Melike Pekmezci2, Arie Perry1,2, Andrew W. Bollen2, Joanna J. Phillips1,2, Steve E. Braunstein5, David R. Raleigh1,5, Philip Theodosopoulos1, Manish K. Aghi1, Edward F. Chang1, Shawn L. Hervey-Jumper1, Joseph F. Costello1, John de Groot1, Nicholas A. Butowski1, Jennifer L. Clarke1,3, Susan M. Chang1, Mitchel S. Berger1, Annette M. Molinaro1, and David A. Solomon2

1. Department of Neurological Surgery, University of California, San Francisco, San Francisco, California, United States 2. Department of Pathology, University of California, San Francisco, San Francisco, California, United States 3. Department of Neurology, University of California, San Francisco, San Francisco, California, United States 4. Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, California, United States 5. Department of Radiation Oncology, University of California, San Francisco, California, United States

Background: Glioblastoma presents as a clinically and molecularly heterogeneous disease, highlighting the importance of identifying novel predictive biomarkers to identify patients who are more likely to respond to targeted treatments.

Materials and Methods: We prospectively conducted genomic profiling on 459 consecutive primary treatment-naïve IDH-wildtype glioblastomas in adults to identify distinct subgroups. The study cohort underwent thorough molecular characterization, encompassing somatic hypermutation analysis, assessment of DNA replication repair deficiency, and DNA methylation profiling.

Results: Among the 459 glioblastomas analyzed, we identified a distinct subgroup (2%, 9/459) characterized by somatic hypermutation and DNA replication repair deficiency resulting from biallelic inactivation of a canonical mismatch repair gene. These tumors frequently harbored deleterious mutations in mismatch repair genes in the germline state, accompanied by somatic inactivation of the remaining allele, suggesting an association with Lynch syndrome. Furthermore, a subset of tumors exhibited proofreading domain mutations in the DNA polymerase POLE, leading to "ultrahypermutation". Histologically, all tumors exhibited features consistent with the giant cell variant of glioblastoma and lacked typical genetic hallmarks of conventional IDH-wildtype glioblastoma, such as EGFR amplification and combined trisomy of chromosome 7 plus monosomy of chromosome 10. Instead, they displayed frequent inactivating mutations in TP53, NF1, PTEN, ATRX, and SETD2, along with recurrent activating mutations in PDGFRA. DNA methylation profiling revealed unique global hypomethylated epigenomes, classifying these tumors as "Diffuse pediatric-type high-grade glioma, RTK1 subtype, subclass A". Notably, five patients treated with immune checkpoint blockade exhibited prolonged survival, with a median overall survival of 36.8 months compared to 15.5 months for the remaining cohort ($p<0.001$).

Conclusions: Our findings underscore the presence of a distinct biological subtype, denoted as "De novo replication repair deficient glioblastoma, IDH-wildtype", within the adult population. These tumors may potentially gain therapeutic advantages from prospective identification and treatment with immune checkpoint blockade.

BTEC 2024 Annual Conference

Survivorship from Pediatric and Adult Brain Tumors

Attendees Listing

Sarah Al Sharie
Faculty of Medicine, Yarmouk University
21163 Irbid
Jordan
Sarahalsharie2000@gmail.com

Karen Alpen
University of Melbourne
207 Bouverie St – Level 3
Parkville, VIC
Australia
Karen.alpen@unimelb.edu.au

Aizpea Artetxe Zurutuza
Biogipuzkoa Health Research Institute
Paseo Dr. Begiristain, s/n
CP 20014
Donostia-San Sebastián
Spain
aizpea.artetxezurutuza@biodonostia.org

Christine Ballard
University of North Carolina, Chapel Hill
4017 Dinsmore Ln
Durham, NC 27704
USA
ballpitt@ad.unc.edu

Luc Bauchet
CHU Gui de Chauliac
80, avenue Augustin Fliche
34000 Montpelier
France
l-bauchet@chu-montpellier.fr

Florien Boele
Leeds Institute of Medical Research
Leeds
United Kingdom
nbrossier@wustl.edu

Julia Botvinov
Hackensack Meridian School of Medicine
2001 N. Soto Street - SSB #230F
23 Robyn Ct.
Emerson, NJ
USA
Julia.botvinov@hmhn.org

Yixin (Stephanie) Chen
UCLA
Los Angeles, CA
USA
stefanichen@hotmail.com

Elizabeth Claus
Yale University
60 College St. LEPH 205
New Haven, CT 06520
USA
elizabeth.claus@yale.edu

Scott Coven
Riley Hospital for Children
705 Riley Hospital Drive
Indianapolis, IN 46202
USA
scoven@iu.edu

Mantas Dmukauskas
National Cancer Institute NIH
9609 Medical Center Drive
Bethesda, MD 20892-9776
USA
mantas.dmukauskas@nih.gov

Eric Durbin
University of Kentucky Markey Cancer Center
2365 Harrodsburg Rd, Ste A230
Lexington, KY 40504
USA
ericd@kcr.uky.edu

Friederike Erdmann
IMBEI
Rhabanusstraße 3/Tower A
55118 Mainz
Germany
friederike.erdmann@uni-mainz.de

Maria Feychting
Karolinska Institutet
Institute of Environmental Medicine
Nobels väg 13
17177 Stockholm
Sweden
maria.feychting@ki.se

Paul Graham Fisher
Stanford University
750 Welch Road
Palo Alto, CA 94304
USA
pfisher@stanford.edu

Jon Foss-Skiftesvik
Rigshospitalet
Blegdamsvej 9
2100 Copenhagen
Denmark
jon.foss-skiftesvik@regionh.dk

Fabio Girardi
London School of Hygiene and Tropical Medicine
London
United Kingdom
Fabio.Girardi@lshtm.ac.uk

Sara Hadad
UCSF
San Francisco, CA
USA
Sara.hadad@ucsf.edu

Johannes A. Hainfellner
Medical University of Vienna
Waehringer Guertel 18-20 # AKH 4J
Vienna 1097
Austria
Johannes.Hainfellner@muv.ac.at

Louise Tram Henriksen
Aarhus University Hospital
Palle Juul-Jensens Boulevard 99
8200 Aarhus N
Denmark
louhen@rm.dk

Thanh Hoang
Baylor College of Medicine
6620 Main St.
Houston, TX 77030
USA
thanh.hoang@bcm.edu

Raoull Hoogendijk
Princess Maxima Center for Pediatric Oncology
Heidelberglaan 25
Utrecht 3584CS
The Netherlands
r.hoogendijk@prinsesmaximacentrum.nl

Bin Huang
University of Kentucky
2365 Harrodsburg Road STE A230
Lexington, KY 40504
USA
Bhuan0@uky.edu

Kimberly J. Johnson
Washington University in St. Louis
One Brookings Dr.
St. Louis, MO 63119
USA
kijohnson@wustl.edu

Christina-Evmorfia Kampitsi
Karolinska Institutet
Stockholm 17177
Sweden
christina.evmorfia.kampitsi@ki.se

Carol Kruchko
Central Brain Tumor Registry of the United States (CBTRUS)
244 East Ogden Ave., Suite 116
Hinsdale, IL 60521
USA
ckcbtrus@aol.com

Ching Lau
The Jackson Laboratory
10 Discovery Dr,
Farmington, CT 06032
USA
ching.lau@jax.org

Angela Lopez-Cortes
University College London (UCL)
30 Guilford Street
WC1N 1EH London
UK
angela.lopez@ucl.ac.uk

Javier Louro
Karolinska Institutet
Nobels väg 13
17177 Stockholm
Sweden
javier.louro@ki.se

Roberta McKean-Cowdin
University of Southern California
1845 N. Soto Street, MC 9239
Soto Street Building Suite 205
Los Angeles, CA 90089
USA
mckeanco@usc.edu

Annette Molinaro
UCSF
1450 3rd Street
San Francisco, CA 94143
USA
annette.molinaro@ucsf.edu

Victoria Mwebe Katasi
Mulago National Referral Hospital
Kampala
Uganda
princess.katasi@gmail.com

Paul Nathan
The Hospital for Sick Children
University of Toronto
Toronto, CA
paul.nathan@sickkids.ca

Kiri Ness
St. Jude Children Research Hospital
262 Danny Thomas Place MS 735
Memphis, TN 38105
USA
kiri.ness@stjude.org

Emily Nissen
University of Kansas Medical Center
3901 Rainbow Blvd, Robinson Hall Suite 5028D
Kansas City, KS 66160
USA
e617n596@kumc.edu

Quinn Ostrom
Duke University School of Medicine
571 Research Drive, MSRB-1, Rm 442
Durham, NC 27710
USA
qostrom@gmail.com

Andrea Pace
IRCCS Regina Elena National Cancer Institute
Neurooncology Unit
Rome, Italy
andrea.pace@ifo.it

Sonia Partap
Stanford University
750 Welch Rd - Suite 317
Palo Alto, CA 94304
USA
spartap@stanford.edu

Mackenzie Prize
Central Brain Tumor Registry of the United States (CBTRUS)
244 East Ogden Ave., Suite 116
Hinsdale, IL 60521
USA
mprice@cbtrus.org

Vidya Puthenpura
Yale School of Medicine
333 Cedar Street
New Haven, CT 06510
USA
vidya.puthenpura@yale.edu

Eduardo Rodriguez
UCSF
San Francisco, CA
USA
eduardo.rodriguez@ucsf.edu

Syed Sarwar
HMH-Jersey Shore University Medical Center,
Neptune, NJ 07753
USA
syed.sarwar@rutgers.edu

Michael Scheurer
Baylor College of Medicine
One Baylor Plaza MS-BCM622
Houston, TX 77030
USA
scheurer@bcm.edu

Joshua D. Strauss
Baylor College of Medicine
1 Baylor Plaza
Houston, TX 77030
USA
joshua.strauss@bcm.edu

Giorgio Tettamanti
Unit of Epidemiology, Institute of Environmental Medicine
Karolinska Institutet
Stockholm
Sweden
giorgio.tettamanti@ki.se

John Villano
University of Kentucky Markey Cancer Center
800 Rose St, CC401
Lexington, KY 40536
USA
jlvillano@uky.edu

Maike Wellbrock
IMBEI
Rhabanusstraße 3/Tower A
55118 Mainz
Germany
mwellbro@uni-mainz.de

Nicole Willmarth
American Brain Tumor Association
8550 W. Bryn Mawr Ave. Suite 550
Chicago, IL 60631
USA
nwillmarth@abta.org

Margaret Wrensch
University of California, San Francisco
1450 3rd St, HD287
San Francisco, CA 94143
USA
mwrensch@yahoo.com

Yan Yuan
University of Alberta
11405 87 Avenue
Edmonton, AB T6G 1C9
Canada
yyuan@ualberta.ca

Brain Tumor Epidemiology Consortium

SAVE THE DATE

2025 BTEC ANNUAL CONFERENCE

MAY 2025

DURHAM, NC - USA