Panel Discussion: Models to advance science and outcomes for Rare CNS tumors

FIGURE

Figure 1. Panelists

Roel Verhaak, Ph.D., Professor and Associate Director of Computational Biology, The Jackson Laboratory **GLASS Consortium (Glioma Longitudinal AnalySiS)** glass-consortium.org	
Why created	Collaborative consortium continuing the work of The Cancer Genome Atlas glioma project. Treatment sensitivity is progressively lost in gliomas; the goal is to determine the genomic factors playing a role in this process.
Stakeholders	Over 100 participants and three publications to date[15,16,17]. Its genomic datasets of longitudinally matched gliomas are publicly accessible for analysis: www.synapse.org/glass.
Accomplishment to date	A high-quality dataset of genomic profiles from longitudinally collected glioma specimens from more than 250 patients was released on November 18, 2019. This dataset is openly available for download and analysis and serves as a resource to the community to study the process of treatment response.
Short-term goal	To expand datasets to more than 500 patients, involving genomic, transcriptomic, and epigenetic data.
Long-term goal	Paradigm-shifting discoveries on how we can better treat patients with a glioma and improve their outcomes.
Martin van de Bent, M.D., Ph.D., Professor and Head of Neuro-oncology at Erasmus MC Cancer Institute **EURACAN (European network for rare adult solid cancer)** https://euracan.ern-net.eu/	

Why created	Created as one of the virtual healthcare European Reference Networks (ERNs) to guarantee patients with rare diseases equal access to good clinical care. They aim to tackle complex or rare diseases and conditions that require highly specialized treatment and concentrated knowledge and resources. EURACAN is aiming at rare cancers, and CNS cancer is one of its 10 domains.
Stakeholders	The EU, national governments, leading EURACAN institution (Leon Berard in Lyon, France; chair Dr. Jean Yves Blay) and a series of institutions throughout Europe.
Accomplishment to date	Development of a virtual web-based consultation program to improve clinical care. Development of European guidelines on rare cancers (medulloblastoma in collaboration with EANO; others in preparation)[18].
Short-term goal	Development of basket trials on rare cancers, in collaboration with EORTC.
Long-term goal	Development of a sustainable network of leading and specialized institutions that allow state-of-the-art care and development of better treatments.
Mark Gilbert, M.D., Chief Senior Investigator, NCCR Deputy Director at the National Cancer Institute, and co-leader of the NCI-CONNECT Program, NOB, CCR, NCI, NIH **NCI-CONNECT (Comprehensive Oncology Network Evaluating Rare CNS Tumors)** cancer.gov/nci-connect **CERN Foundation** cern-foundation.org	
Why created	CERN: created in 2007 to address an unmet need for new treatments for patients with ependymoma. Enabled the development of a collaborative network of clinical and laboratory-based experts in pediatric and adult ependymoma. NCI-CONNECT: created in 2017. Dr. Terri Armstrong and Dr. Mark Gilbert leveraged their experience from their leadership of CERN to create a national research network to study rare CNS cancers and run clinical and translational studies.

Stakeholders	CERN: supported by philanthropy enabling the creation of clinical trial networks and the largest repository of clinically annotated ependymoma samples (foundation for several seminal investigations). Funding was also provided to select laboratories to advance scientific endeavors related to ependymoma biology and treatment. NCI-CONNECT: support from the Cancer Moonshot℠. There are now 32 national brain tumor centers of excellence in the United States involved, with the Neuro-Oncology Branch at the NCI being the lead center. Patients are encouraged to participate either remotely (web-based enrollment) or with personal visits. All evaluations and molecular testing related to NCI-CONNECT are provided without cost.
Accomplishment to date	CERN: Tumor Tissue Repository; first prospective clinical trial in adult recurrent ependymoma (treatment now incorporated into the NCCN guidelines)[19]. NCI-CONNECT: consensus workshops for rare CNS cancers including histone mutated glioma, medulloblastoma, ependymoma and oligodendroglioma. Several meeting reports containing roadmaps for future investigations have been published[20,21,22].
Short-term goal	CERN: outreach and education; now part of the National Brain Tumor Society. NCI-CONNECT: complete accrual to a multi-center immunotherapy protocol for patients with rare cancers.
Long-term goal	CERN: outreach and education. NCI-CONNECT: launch additional clinical trials including ONC206, an agent with potential efficacy in histone mutated tumors; accrual of tumor samples for a rare CNS cancer repository to enable in-depth molecular analysis and provide greater insight into these diseases and potentially lead to new therapies.

Richard Gilbertson, Ph.D., Li Ka Shing Chair of Oncology and Head of the Department of Oncology at Cancer Research UK Cambridge Center **Medulloblastoma in the Mountains** https://www.crukchildrensbraintumourcentre.org/meetings/medulloblastoma-in-the-mountains-mim/ **Ependymoma Consensus Meeting**	
Why created	The meetings were created because the pediatric community is small, and these diseases are rare. Advances for these rare diseases depend on open sharing of ideas and progress. The key is bringing the community together pre-publication to do this.
Stakeholders	Academic and clinical communities; Cancer Research UK, the Brain Tumor Charity, and other brain tumor foundations, along with universities.
Accomplishment to date	Published consensus statements on the molecular classifications of medulloblastoma and ependymoma[23,24]. These underpin the current WHO classification of brain tumors.
Short-term goal	Formation of teams for grant applications (e.g. Grand Challenge).
Long-term goal	Establish international clinical trials.
Elizabeth Claus, M.D., Ph.D., Professor of Biostatistics and Neurosurgery at Yale University and Attending Neurosurgeon and Director of stereotactic radiosurgery in the Department of Neurosurgery at the Brigham and Women's Hospital **Low Grade Glioma Registry** https://lggregistry.wixsite.com/study	
Why created	Lack of large-scale study of Lower Grade (Grade II/III) Glioma (LGG), a uniformly deadly brain tumor that is estimated to affect over 30,000 persons in the United States. Treatment options and survival times have not significantly changed over the past forty years, no environmental exposures have been consistently linked to risk (other than high doses of ionizing radiation) and the optimal treatment regime remains unclear.

Stakeholders	Multiple, including: 1) the two major brain tumor patient organizations in the United States, the American Brain Tumor Association (ABTA) and the National Brain Tumor Society (NBTS); 2) many of the internationally based brain tumor patient organizations including the International Brain Tumor Alliance (IBTA) in the United Kingdom and the STOPBRAINTUMORSNOW (nlhersontumor.nl) located in the Netherlands; 3) numerous patient advocates/advocacy groups including one of the Brain Tumor Social Media (#BTSM) organizers/members and patient researcher Ms. Liz Salmi; 4) the LOGLIO Collective sponsored by the Dabbiere family; and 5) the NCI-CONNECT Program at NIH.
Accomplishment to date	Enrolled over 400 participants from over 30 states and 15 countries.
Short-term goal	Continue to enroll patients and work towards high-level funding.
Long-term goal	Better describe the molecular trajectory of LGG and use this information to better select treatments. Better understand and eliminate the barriers to patient participation in LGG research and increase the diversity of participants in the Registry.
Erin Dunbar, M.D., Director of Neuro-oncology at the Brain Tumor Center at Piedmont Healthcare **Real World Experience – Taking care of patients with rare CNS tumors**	
Challenges	Include: • Providers have to seek help outside of their institution because of limited own experience during training and low number of close mentors/colleagues to go to. • Patient heterogeneity, including presentation, molecular/genetics, prior treatments, comorbidities, thus makes selecting/managing treatments complicated • Lack of high-level evidence (e.g., NCCN level 1, cat A), limiting both a clear treatment path and confidence. • Lack of insurance approval for treatments suggested by the literature or experts. • Lack of trials and registries. • Lack of knowledge on how to manage the patient at diagnosis and across the disease continuum. • Lack of education for patients and caregivers • Lack of resources and support for both providers, patients, and their practices/hospitals. Little social and financial services.

Optimal care	Involves: • Connecting with "lifeline" experts, e.g. NCI-CONNECT • Provider self-education; collecting and disseminating education and resources for patients, caregivers, and practice/colleagues/institution. • Being a trial investigator and steer all patients/colleagues to seek trials/registries for all patients. Work to have as many trials as possible in my institution/region. • Advocating for access to trials and non-regulatory approved treatments on my institution/region. • Volunteering in patient, government and society forums that advocate for access to care and resources for care. • Committing to training and encouraging the next generation to care for, and advocate for, the advancement of care for rare tumors. • Contributing to the literature.
Improving current care	Would involve: • More trials with easier inclusion criteria, e.g., basket-trials, response adaptive randomization platform trials, registries sponsored by pharma/philanthropy. • More access to drugs or treatments, outside of trials, whether via expanded access or "right to try" with the caveat of sufficiently qualified providers are directly involved in the selecting and monitoring of the drug or treatment. • More philanthropic support for patients, providers, caregivers in areas of education, access to trials, and care coordination. • Insurance and/or philanthropic support for Telehealth. Funding research for outcomes research with Telehealth. • Tumor-specific education for patients, caregivers, and practice/institutions. • More government and private resources and support for specific tumors that could be accessed by patients, caregiver and practice/institutions. • Incentives for training in rare tumors, attending education forums, contributing to the literature, proposing research, etc. • Effective mentoring of trainees and young professionals. • Lowering logistical barriers to pharmacy investing in rare tumor research without compromising safety/data.

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