



Research Roundtable

July 20, 2023

“Use of External Control Data in Brain Tumor Clinical Trials”

The 11th Research Roundtable took place on July 20, 2023, as a multi-stakeholder, multi-disciplinary group of distinguished pediatric brain tumor experts, statisticians, industry leaders, regulator officials, and patient/caregiver representatives convened for a full-day, in-person meeting focused on the use of external control arms in brain tumor clinical trials.

Tresa Spencer, Patient Advocate, provided her perspective on leveraging the power of external data in brain tumor clinical trials to enable faster access for patients to innovative treatments. She emphasized the importance of clinical trials for patients and the hope they bring while highlighting several barriers and challenges faced by patients in accessing and participating in clinical trials, including:

- Lack of knowledge about trials and where to find information
- Limited access to trials, especially for patients at regional medical centers
- The impact of disease progression on limiting patients from participating in certain trials
- The impact of certain prior treatments (like Avastin), which can exclude patients from participating in trials

The main themes of the meeting were:

- Patients with brain tumors are eager to accelerate clinical trials and drug development, but they face barriers in participating in clinical trials and may be hesitant to enroll in a randomized study if the control arm relies on an ineffective standard of care.

- Use of external controls is complex, and there is no one-size-fits-all approach. However, there are circumstances where real-world evidence can and should be used in drug development, leveraging opportunities for externally controlled and hybrid design trials.
- Sponsors and investigators need to ensure careful planning and consultation with the FDA to ensure the validity and reliability of study findings.
- While recruitment of pediatric brain tumor trials is extremely challenging, especially in the context of rare diseases like atypical teratoid rhabdoid tumor (ATRT), efforts underway to develop an ATRT registry and design a platform trial using external control cohorts demonstrate a promising approach to overcoming barriers and advancing innovative solutions.
- Advancing initiatives to develop a registry and leverage its data for external controls in a rare pediatric tumor setting demonstrates an opportunity for a successful model. These efforts highlight the significance of data sharing, patient engagement, thoughtful trial design, collaboration, creativity, and a patient-centered focus in clinical research.
- In the adult setting, high-grade glioma (GBM) provides an opportunity and a need to consider use of external control data.
- There are models being developed to gather and appropriately combine data from prior clinical trials and real-world data to develop datasets that could be used as external controls.
- There are multiple statistical approaches and trial design options that can be used to alleviate potential limitations of external control data within clinical trials.
- In the GBM space, GBM AGILE is demonstrating the opportunities for using internal controls through a platform trial and developing data that can be used in future studies. Additionally, one company is currently advancing a registration study in recurrent GBM using external control data.
- Retrospective and prospective validation of datasets are important. The adult neuro-oncology field should commit to data sharing and prospective validation to create external control data for use in future studies.
- Reliable external controls can lead to faster trial outcomes, more regulatory approvals, and better treatment options for patients with rare central nervous system (CNS) cancers.
- Multiple models for data sharing exist; however, barriers remain. The field must commit to sharing clinical trial data and creating a centralized database to facilitate research and accelerate progress in brain tumor treatments. Patients and advocates emphasize the importance of data sharing to advance science and improve outcomes.
- There is an urgent need for more effective treatments and trial designs to address the high failure rates and limited options available for patients with brain tumors. Participants stressed the need to consider patients' preferences and needs when designing clinical trials and developing treatment approaches.

Key takeaways from the meeting included:

- Patients and care partners want their data to be used for future clinical trials and overcoming barriers to clinical trials, especially in cases of rare diseases with high mortality rates.
- External control arms have significant potential for adult brain tumor trials, with a role for artificial intelligence (AI) and machine learning in developing capacity.
- The brain tumor field needs to achieve consensus on developing the capacity and knowledge for using clinical trials, uncertainty levels, and challenges in determining the perfect external control.
- Proposed action and next steps include working with the FDA, cooperative groups, and industry to establish and incentivize a data-sharing network, implementing a multi-stakeholder collaborative study to prospectively assess the validity of using external control data and statistical methodologies in clinical trials, revising consents to allow data use for future trials, and educating patients about the value of data sharing.