



**December 11, 2020**

## **Moving the Needle—Progress for Brain Tumor Clinical Trials**

*Roundtable participants include clinicians, researchers, representatives of biopharmaceutical companies, patients, patient advocates, and regulators.*

**PURPOSE:** To follow up on action items and discussion related to advancing the vision for hybrid, decentralized brain tumor trials ([see July 24, 2020 Research Roundtable summary](#)) and to developing a proof-of-concept study for a novel imaging endpoint for high-grade brain tumors ([see December 13, 2019 Research Roundtable summary](#)).

### **Key topics included:**

- Updates on efforts to decentralize brain tumor clinical trials
- Group discussion and refinement of a proof-of-concept study design to develop and validate a “rate of growth” imaging endpoint for high-grade brain tumors
- Group discussion to identify and prioritize topics for 2021 Research Roundtable meetings

### **Major conclusions included:**

#### *Advancing Progress Toward Decentralized/Hybrid Brain Tumor Clinical Trials*

- NBTS is catalyzing a variety of neuro-oncology-specific issues to advance progress toward decentralized/hybrid clinical trials.
- FDA has been considering the issue of heterogeneity and imaging interpretation in the setting of decentralized trials where multiple sites and protocols are being used. One potential solution to issues of heterogeneity and imaging interpretation may be to use a standardized protocol to collect and analyze imaging.
- Possible means to progress toward decentralized/hybrid clinical trials include:
  - Comparison of how providers are conducting virtual neuro-oncology exams, evaluating and potentially adapting the American Academy of Neurology guidance on virtual exams, and/or developing specific neuro-oncology guidance for incorporating these into future trials in a post-COVID environment.

- o Development of a downloadable Brain Tumor Imaging Protocol (BTIP) card for patients (or even a QR code to use) to bring to their MRI exams to make sure that they are receiving standardized imaging protocols. This resource can be distributed widely by NBTIS, Society for Neuro-Oncology, and other organizations.
- o Development of a whitepaper or publication that addresses e-consent and 1572 issues that could be used to inform Institutional Review Boards (IRBs).
- This type of publication could be used as a resource for IRBs of record and contract research organizations (CROs) to feel supported by expert opinion.
  - o Incorporating a radiologist as an investigator at a study's central institution and creating a means for reimbursement of their time to provide formal interpretations.

### *Developing a Novel Imaging Endpoint*

- It's important for the scientific community to provide a general framework for novel imaging endpoints and for sponsors to implement these into study designs (even as secondary endpoints) to provide high-quality data to support validation of the surrogacy and enable regulatory evaluation toward the eventual use as primary endpoints.
- Additional data is needed to provide confidence that responses recorded via imaging are truly responses.
  - o This is especially true if there is clear evidence of tumor growth coming into a trial and the tumor is seen to be stable or shrinking after therapy.
  - o There is merit to getting additional scans pre-treatment, as well as specifically getting a scan immediately before treatment begins.
- Some tumors are so aggressive that delays between initial scans and treatment initiation can be a significant confounding factor for evaluating the impact of an investigational therapy. It is important to try and reduce these delays as much as possible.
- Sponsors will be interested in an effort to develop imaging endpoints, especially if issues of standardization, cost, and regulatory support are addressed.
- Near-term opportunities for implementation of an imaging proof-of-concept trial include compiling existing datasets from academic institutions, adding the protocol to arms in the GBM AGILE platform trial, and leveraging National Clinical Trials Network (NCTN) studies through the National Cancer Institute (NCI).
- Concrete steps to move forward with an imaging endpoint include:
  - o Evaluating this approach in the recurrent glioblastoma (rGBM) setting by gathering imaging data that can demonstrate whether, and how fast, the tumor is growing coming into the study and at multiple time points during treatment.
  - o Conducting both retrospective (natural history) trial assessments and prospective proof-of-concept trial assessments.
  - o Using tissue sampling in the proof-of-concept study to enhance the argument for validity of a novel imaging endpoint.

- o Combining this proof-of-concept trial with measures of clinical function from the patient perspective by also evaluating growth rate in terms of how the person feels and functions.