Developing a Roadmap for Use of Performance-Based Cognitive Function Clinical Outcome Assessments in Neuro-Oncology Clinical Trials for Newly Diagnosed GBM

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National Brain Tumor Society convened a multi-stakeholder, multi-disciplinary group of distinguished brain tumor experts, industry leaders, regulatory officials, and patient and care partner representatives convened for a virtual five-hour roundtable meeting focused on Developing a Roadmap for Use of Performance-Based Cognitive Function Clinical Outcome Assessments in Neuro-Oncology Clinical Trials for Newly Diagnosed GBM. The goal of this Research Roundtable was to enhance opportunities for the use of performance-based neurocognitive function clinical outcome assessments (COAs) in clinical trials for patients with newly diagnosed glioblastoma (GBM) and encourage consistent use of COAs in neuro-oncology drug development. This meeting was designed to understand and address barriers to the goal of incorporating key measures of neurocognitive function in these trials as efficacy endpoints.

Key Themes and Opportunities for Progress

Importance of Neurocognitive Assessments

Patients highly value treatments that preserve neurocognitive functions such as memory, as highlighted by a 2014-2015 survey of 1,700 patients with brain tumors and caregivers and reinforced by patient advocates. Neurocognitive testing is critical for understanding treatment effects, quality of life, and survival outcomes. These assessments provide essential insights into patient functioning over time and at key treatment milestones. There should be a focus on relevant and reliable concepts for assessment. Studies should use fit-for-purpose, objective measures. FDA should be engaged early to optimize endpoints and methods. Support for patient-centered treatment development aligns with the 2012 PDUFA patient-focused drug development initiative. There are validated tools for clinical and trial settings. It is important to assess

neurocognitive outcomes both at specific time points and over treatment trajectories. There should be routine inclusion of neurocognitive endpoints in all phase III trials. In the context of multi-site clinical trials, a full neuropsychological assessment is unrealistic, but an abbreviated, disseminatable approach exists that can be applied in any setting. There are challenges associated with missing data, but there are strategies for better data collection and categorization.

Participants discussed possible future activities:

- **Educational Outreach:** There could be increased collaboration with professional societies to create continuing medical education (CME) opportunities and raise awareness about the importance of neurocognitive testing in clinical trials.
- **Advocacy for Data Sharing**: Promote data accessibility to enable meaningful analyses that inform trial design and endpoints. Target cooperative groups and regulatory bodies to push for routine data sharing to investigators with appropriate expertise.
- **Standardization in Trials**: Establish neurocognitive testing as a baseline standard in all phase III trials. Work toward integrating these measures in earlier trial phases where feasible.
- **Expanding Relevance Beyond GBM**: Extend neurocognitive testing to other neuro-oncology areas, such as brain metastases, in which neurocognitive outcomes have already impacted standard of care treatment decisions.
- **Flexibility in Trial Design**: Leverage lessons from COVID-era hybrid trials to integrate neurocognitive testing into flexible, decentralized models. Facilitate broader participation and data collection across clinical settings.
- **Quantifying Value**: Articulate the cost and value of neurocognitive testing to secure funding and institutional support.
- **Technological Innovation**: Continue exploring experimental tools (e.g., apps, wearables) to enhance measurement of cognition with potentially less patient burden.