National Brain Tumor Society

Research Roundtable

Prospects for Use of Liquid Biopsy in Neuro-Oncology

July 18, 2024

On July 18, 2024, a multidisciplinary group of distinguished brain tumor experts, industry leaders, regulatory officials, and patient/caregiver representatives convened for a Research Roundtable meeting focused on **the use of liquid biopsy in neuro-oncology.** The goal of this NBTS Research Roundtable was to evaluate prospects – both opportunities and challenges – of using liquid biopsy to advance neuro-oncology drug development and diagnostics. Discussions included clarification of definitions, understanding regulatory perspectives, and consideration of various modalities ranging from the use of cerebrospinal fluid (CSF) and blood, to multi-omic approaches. Desired outcomes included consensus prioritization of important next steps for advancing progress.

Key Takeaways

- Liquid biopsy has potential to advance the field of neuro-oncology therapy development, however it is not viewed as a replacement for current tumor biopsy and imaging techniques. Rather, it should be seen as an additional tool in the toolbox for clinicians, investigators, sponsors, regulators, and patients.
- FDA is interested in Circulating tumor DNA (ctDNA) for early drug development, molecular profiling, monitoring residual disease, and assessing investigational product response. CtDNA has shown promise as a prognostic biomarker in early-stage disease, and several studies have indicated worse outcomes for patients with detectable ctDNA compared to those without detectable ctDNA after first-line therapy.
- Current FDA Guidance in this area was published in May 2022 and addresses four main regulatory uses: patient selection, residual disease detection, response measurement, and early endpoints.
- Early-phase clinical trials should include ctDNA endpoints alongside traditional efficacy endpoints.
- There is a need to align academic research with regulatory guidance to ensure research is on a path toward regulatory acceptance. Academic institutions should partner with

industry and regulatory bodies to design studies that could lead to regulatory approval and clinical validation of liquid biopsy assays.

- There is a concern about the current regulatory and diagnostic landscape, which may not fully integrate liquid biopsy results into global registration trials. This creates uncertainty about how these results can be utilized for regulatory approvals.
- There is the need to leverage big datasets from various trials and studies. Data standardization is crucial for creating robust datasets beneficial for regulatory and drug development purposes. There are opportunities to leverage existing platforms and data from major institutions through robust collaborations.
- There is also a need to standardize factors such as sample collection, processing, storage, and analysis approaches for liquid biopsy efforts to ensure consistency in clinical trials. There is potential in creating a collective "lab notebook" for processing samples and sharing data among institutions. This approach could maximize the use of available resources and improve research outcomes.
- The traditional liquid biopsy validation framework includes analytical validity, clinical validity, and clinical utility. Patient feasibility should be considered as a fourth element, highlighting the importance of incorporating patient perspectives in research frameworks.
- It may make sense for the neuro-oncology field to focus, first, on specific disease settings, such as glioblastoma (GBM) and leptomeningeal metastasis, to develop standardized protocols and build on existing standards of care.
- CSF biopsy is more advanced than plasma or blood for neuro-oncology due to higher yield and clearer signal. Blood biopsy can be developed for the future, with ongoing efforts to reduce signal-to-noise ratios and enhance tumor-associated liquid biomarkers. Utilizing existing data from small-scale studies and collaborating with companies that have already conducted preliminary research on CSF samples can help build a case for larger-scale studies and clinical validation.

Future Implementation and Path Forward

There is a significant need to educate healthcare professionals, patients, advocates, and caregivers about advancements in CSF and blood biopsy. There are opportunities to leverage existing initiatives like NBTS's MyTumorID program to enhance the community's understanding of biomarkers.

A multidisciplinary approach involving oncologists, neurosurgeons, researchers, and patient advocates is needed to drive the advancement of liquid biopsy techniques and their integration into clinical practice. Engaging patient advocacy groups can help in normalizing procedures like lumbar punctures and biopsies, which are often perceived as risky. Advocacy statements from patient groups can support the push for these procedures to be considered part of the standard of care.

Funding for ongoing research and education in these areas is critical to advancing progress in bringing liquid biopsy to neuro-oncology. Advocacy is needed to support stable, long-term federal funding (e.g., from NCI).