2024 Brain Tumor Leaders Strategic Fly-In

1. **Purpose**

This year's 3rd Annual Brain Tumor Organization's Leadership Fly-In was dedicated to advancing the understanding and implementation of molecular profiling in the treatment of brain tumors. This event brings together leaders in the field—clinicians, researchers, advocates, and nonprofit leaders to foster collaboration and accelerate the adoption of molecular profiling as a standard practice at diagnosis. By sharing insights, discussing challenges, and exploring innovative solutions, we aim to improve patient outcomes through personalized treatment approaches and informed decision-making. Our collective efforts will contribute to a future where every patient receives the most precise and effective care possible.

2. **Participants**

Thirty-eight individuals, representing twenty-three organizations and healthcare systems were in attendance.

3. **Outcomes**

Following insightful scientific presentations and dynamic breakout sessions, which are summarized below, attendees reached a consensus on the critical need for an educational campaign targeting both patients and healthcare providers.

The recommended campaign aims to enhance awareness and understanding of molecular profiling as a pivotal tool in ensuring patients have a correct diagnosis and prognosis as well as a tool for personalizing brain tumor treatment. By focusing on the importance of early molecular diagnostics, the campaign will advocate for the integration of molecular profiling into standard care protocols, ensuring that patients receive the correct diagnosis with the most informed and effective treatment options from the outset.

Attendees emphasized that this initiative should include clear, accessible information for patients and caregivers, as well as detailed guidance and resources for healthcare providers. The goal is to bridge the knowledge gap, enabling informed decision-making that can lead to improved outcomes and quality of life for brain tumor patients.

The collective agreement to develop this educational campaign marks a significant step forward in the fight against brain tumors, reflecting the shared commitment of all attendees to advancing patient care through education and innovation. A follow-up call is scheduled in September to begin to discuss next steps.

3. **Summary of Panel Discussions**

Kelli Duprey, Executive Director of Our Brain Bank; Laura Hynes, Executive Director of the Brain Tumor Network (BTN), and Kim Wallgren, Executive Director of the Collaborative Ependymoma Research Network (CERN), a program of The National Brain Tumor Society (NBTS), introduced the topic of molecular profiling to attendees and each shared data from patient studies.

Our Brain Bank found that 32% of patients surveyed were not informed about tumor testing prior to their initial surgery, and some were never informed. 69% of patients were not informed about storing tissue for future testing and 79% reported not having their tissue stored for possible treatments or clinical trial qualification. 52% of patients surveyed reported no discussion of seeking a second opinion and 64% reported not being offered enrollment in any clinical trial.

BTN sent a 10-question survey to all patients who have been diagnosed with a grade III/grade IV tumor in the last 2 years who have contacted BTN. Of the 127 respondents, 23.7% responded that they did not have molecular profiling performed. Of those who did have molecular profiling done, 37.9% said the results of the test were not explained to them. Additionally, 64.4% of the patients said they were not presented clinical trials as a treatment option.

NBTS conducted a community needs assessment and found that 30.8% of patients surveyed reported a minimal understanding of biomarker testing, and only 29% of patients had biomarker testing performed. Of those for whom biomarker testing was not performed, the top reason identified for such was "the doctor of care team did not mention biomarker testing as an option." Additionally, 60.5% of patients surveyed reported that their doctor or care team never discussed clinical trials as a potential treatment option for their tumor and 84.3% of patients reported that they have never participated in a clinical trial. Of those who have never participated in a clinical trial, 44.8% of patients reported the reason for such was that their doctor or care team never discussed clinical trials with them.

After learning of the results of these surveys earlier in the year, the organizers wanted to convene this panel to highlight the need for equitable access to education and standardization of molecular testing in neuro-oncology treatment protocols; to understand the current set of the field; and then begin the work of determining the best opportunities to help to continue to move the field forward for the benefit of patients.

Nicole Wilmarth, PhD, Chief Mission Officer, ABTA and Scott Davis, PhD, Managing Director, Sontag Innovation Fund, moderated a panel discussion on the current state of the field of molecular profiling. The panelists were Dr. Craig Horbinski, Northwestern; Dr. Matija Snuderl, NYU; Dr. Michael Vogelbaum, Moffit Cancer Center; Dr. Chetan Bettegowda, Johns Hopkins; and Dr. Ashley Ghiaseddin, University of Florida.

The panel focused on molecular testing for glioma patients, including how molecular profiling is currently being used, the future opportunities for implementing molecular profiling into clinical practice, and what standards should be established to best serve patients and their families.

A. <u>Molecular Profiling Basics</u>

Dr. Craig Horbinski presented the first panel talk that focused on the basics of molecular profiling. In this talk, he mentioned the typical profiling techniques that are used for brain tumors: (1) next generation sequencing to screen for mutations; (2) fusion screening to look for pathologic fusions; (3) copy number arrays to screen for gains and losses across the genome; (4) MGMT promoter methylation testing to determine whether the MGMT gene is silenced; and (5)

genomic DNA methylation profiling to determine what parts of the entire genome are methylated or not.

Dr. Horbinski presented on the significant role molecular profiling plays in tumor diagnosis, including the many altered genes that are present in various brain tumors (e.g. BRAF, NTRK, IDH). In approximately 50% of cases, molecular profiling can improve patient care by altering diagnosis or prognosis, identify a druggable target, or both. He has a paper currently pending publication that will provide additional information on this topic.

B. Molecular Profiling Impact on Care and Clinical Trials

Dr. Ashley Ghiaseddin presented the second panel talk that focused on the impact of molecular profiling on patient care, including clinical trials. In this talk, he discussed how molecular profiling can provide diagnostic and prognostic information, especially when histology is unable to differentiate tumors. In addition, profiling can inform clinical trial enrollment, including improving the speed of eligibility determination and helping with enrollment of patients that more closely resemble each other, which could improve reproducibility in the real-world setting. Regarding clinical trials, if driver mutations (e.g. BRAFV600E, IDH, NTRK fusions) are identified for which a therapy or clinical trial is available, this information can be provided to the patient, allowing the patient to be better informed about the most appropriate treatment or trial for them. Dr. Ghiaseddin also presented a slide containing a table (Table 1) from Alyx Porter et al., (2023) , which showed a number of relevant glioma targets that respond to therapy in some patients, highlighting the importance for patients today, but also noted that the value of testing will continue to increase as more targeted therapies are developed.

C. Tissue Collection & Storage

Dr. Michael Vogelbaum then talked about tissue collection and storage for his panel presentation. There are ongoing efforts to promote Window of Opportunity (WoO) or Phase 0 studies, where sampling can be performed from the blood, CSF, tumor tissue, and/or tumor infiltrated brain. Current challenges of tissue collection in WoO/Phase 0 include developing a pre-surgical dosing plan, issues regarding PK/PD analysis, establishing a scientific control for the tissues, payment challenges, frequency of sampling and where to obtain the sample. Work is underway to develop an intraoperative database for multi-modality data capture to “geotag” tissue collection, with preliminary results suggesting that additional follow-up studies should be performed. In addition, a biospecimen working group is being developed to focus on development of protocols for longitudinal tissue sampling. There remain challenges of standardization, processing, storage and allocation of tissue, in addition to payment challenges for longitudinal sampling.

D. Innovations Impacting Molecular Profiling in the Brain Tumor Space

Dr. Chetan Bettagowda provided the next panel presentation, focusing on innovations impacting molecular profiling in the brain tumor space. Imaging was discussed first, utilizing an example from Hollon et al., 2020. This paper demonstrated an intraoperative imaging technique on tissue utilizing machine learning algorithms to predict diagnosis at the bedside in near real-time

automated fashion. Further, developments in intraoperative molecular profiling were discussed, which could be used to help profile tumors during surgery. Finally, Dr. Bettagowda discussed advancements in liquid biopsy which could be used for many purposes included testing drug response and evaluating minimal residual disease.

E. Patient Education and Advocacy

Wrapping up the panel talks, Dr. Matija Snuderl talked about patient education and advocacy in the molecular profiling space. He began by challenging the panelists to think about what the minimal diagnostic standard should be and how we as a brain tumor community can work to ensure access to patients in terms of cost and site of care. Regarding diagnosis, a histology only diagnosis can be incorrect 15% of the time, where methylation profiling is now emerging as an important benchmark for diagnostic accuracy. The new regulatory framework was also mentioned, where the FDA has announced its intent to regulate Laboratory Develop Tests (LDT) as medical devices. This initiative is a large departure from current standards of LDTs, and if upheld could drastically increase costs for companies, stifle innovation and pressure test the resources of the FDA. Ultimately, this could decrease patient access to molecular testing and limit innovation. One alternative solution would be for the government to, instead, rely on current inspection processes such as the College of American Pathologists (CAP) accreditation process.

4. **Summary of Breakout Sessions:**

After the panel discussion, attendees heard a presentation from Julie Fleshman, President and CEO of PanCan and Fatima Zelada-Arenas, Senior Director, Patient Services, Research, and Education for PanCan, who spoke about their organization's *Know Your Tumor* program and how it is benefiting pancreatic cancer patients and improving patient care and outcomes. https://pancan.org/facing-pancreatic-cancer/patient-services/know-your-tumor/

Attendees then broke into three small groups to begin discussions about how the nonprofit community can better align to make sure that brain tumor patients receive adequate education and information about molecular profiling, tissue sampling, and clinical trials, prior to making treatment decisions. The topics for discussion included identification of barriers to brain tumor patients receiving molecular profiling prior to care decisions; key elements of an educational campaign; and how to measure success. The breakout groups identified a lack of baseline education as a major barrier to widespread adoption of molecular testing. Specifically, there is a need for clear educational resources that describe, in a patient-friendly way, what molecular profiling is, how does it impact treatment decisions, where can you have it done, and who will pay it? Break out groups also raised other barriers that should be considered such as insurance coverage, geographical barriers, clinical variability in testing, delays in receiving test results, and provider aptitude to order because of lack of current treatment options. A complete list of breakout group responses can be found in the attachment at the end of this document.

The breakout groups all saw the value of creating an educational campaign that would provide uniform communication for patients. Several groups mentioned the need for targeted messages for certain populations and collaborating with aligned organizations to elevate the message.

There are additional considerations in the breakout group responses that should be considered when structuring a campaign.

Finally, the breakout groups discussed how to measure success. The groups all recognized the need to set goals with regular assessments overtime. There were several suggestions to engage outside entities such as testing companies or site-specific data to gauge increase in testing.

5. **<u>Next Steps</u>**

As a follow-up to the discussions at the fly-in, the brain tumor organization's leadership team will reconvene in September to identify concrete action items, with the understanding that this may not be a priority for all members and thus a smaller working group may form. Potential focus areas may include the following priorities:

A. Co-marketed Educational Campaign

a. Develop a collaborative, co-branded initiative aimed at educating patients on the importance of:

i. Molecular profiling as part of their diagnosis and treatment planning.

ii. Tissue storage options for future research and treatment opportunities.

iii. Clinical trials, including how to find and discuss them with healthcare providers.

B. Stakeholder Engagement

a. Identify key stakeholders, including healthcare providers, testing companies, insurers, advocacy groups, and patient organizations, to collaborate in promoting these educational efforts.

C. Resource Development

a. Begin identifying existing materials and resources and when necessary, drafting new materials that will serve as the foundation of the campaign, ensuring they are accessible, patient-friendly, and scientifically accurate.

b. Identify potential funding sources for campaign.

D. Timeline and Metrics

a. Establish a timeline for campaign roll-out and determine metrics to measure the impact on patient knowledge and clinical outcomes, as well as barriers to patients' ability to access such resources.

Attachment 1

Breakout Group 1

I. Barriers
   1. Baseline Education- What is it? How does it affect my treatment?
   2. Cost- is it covered by insurance? What are the alternatives if it is not covered?

II. Educational Campaign
   1. One Brand
   2. Resources located in ERs/Urgent Care (are there societies to connect?)
   3. Opportunities to collaborate with heath care providers
      a. Oncology Nurses
      b. ER Nurses
      c. Case Management
      d. Social Works
      e. Pharmacies/Pharmacists
   4. Key messages/formats
      a. Acronyms defined
      b. Checklist- branded by advocate coalition
      c. Reporting capabilities
      d. Survey

III. How to measure success of campaign
   1. Increased number of referrals made for comprehensive tumor testing
   2. How did you hear about us?

Breakout Group 2

I. Barriers
   1. Access
   2. Cost
   3. Lack of Accessibility

4. Variability of Institutional Procedures and Capability
5. Delays due to various issues like second opinions, tissue access, etc.
6. Lack of clarity and consensus on mandatory tumor testing

II. Education Campaign

1. Take a collective stand on major issues (i.e. testing, impact on treatment decisions)
2. Uniform communication on direction and roadmap for patients
3. Collaboration for educational campaign
    a. Determine who would like to be involved
    b. ID all pieces of the puzzle and make sure parties are involved.
    c. Cohesive language in law terms adopted and used by all parties
    d. SNO Academic Guidelines papers est. consensus; NCCN guidelines committee

III. Key Messages

1. Consensus paper on necessary testing
2. Projects that elevate collective voice (ACS/CDC/Brain Act)
3. Involve testing companies
    a. Advertising dollars in community missed opportunity

IV. Measuring Impact & Success

1. Continue to survey community
2. Engage CBTRUS to add molecular profiling data in future
3. Work with testing company or site-specific data to gauge increase
4. Clinical trial networks, like GBM Agile enrollment data

Breakout Group 3

I. Barriers

1. Tissue availability and accessibility
2. Geographical Barriers (rural)
3. Insurance
4. Understanding “why”- benefits/direction
5. Clinical variability

6. Timing of process- delays timeline
7. Heterogeneity of tumor
8. Provider aptitude to order because of lack of treatment options to justify ordering the testing

II. Education

1. Build an online tool/portal (generative AI)
2. Collaborate with aligned organizations, HCPs on the standard basic testing that should be completed
    a. Multi-organizational messaging to show importance and collective voice
3. Targeted messaging for certain populations
    a. Recognizing potential cognitive defects
    b. Caregiver messaging
    c. Unique cultural or geographic populations

i. Who is involved in care decisions and how decisions are made?

4. Different forms of media from analog to AI
    a. Different learning styles
    b. Engaging, interactive
5. Building trust
    a. Simple language and format
    b. Benefit of an intermediary/navigator

III. Metrics

1. Need baseline, but increase in molecular testing
2. Surveys
3. Centralized data collection
    a. Accessible
    b. Tracking/follow-up
4. Set goals with regular assessment over time
    a. Adapt as required
5. Open sharing of resources and efforts among aligned organizations