Primary Central Nervous System Tumors (CNST) demonstrate remarkable intra-tumoral and inter-tumoral heterogeneity contributing to therapeutic resistance. We report implementation of a PMRP for patients with primary CNST as part of the Swedish Cancer Institute genomics program.

**METHODS**

An Institutional Review Board approved prospective registration protocol was activated in September 2014 as a data repository for cancer patients undergoing genomic evaluation as part of the Swedish Cancer Institute PMRP. NGS profiling of activated in September 2014 as a data repository for cancer patients undergoing genomic evaluation as part of the Swedish Cancer Institute PMRP. NGS profiling of CNST was performed using a 68-gene alteration panel (Figure 1). Mutations (M) were classified as:

- Actionable (approved clinical indication)
- Applicable (clinical trials or off-label indication)
- Unknown significance

As of December 2015, sequencing was completed on 98 patients with primary CNST. Diagnoses included: glioblastoma (51), anaplastic glioma (25), low-grade glioma (7), neuronal-gliai tumors (4), DLBCL (3), medulloblastoma (3), ependymoma (1), hemangiopericytoma (1), meningioma (2), pituitary adenoma (1). Mutations were identified in 97% of cases.

**RESULTS**

The most common Applicable (M) (number of mutations/variants) included:

- TP53 (33), IDH1 (31), Pten (14), TMY3 (10), EGFR (8), TPMT (8), PIK3CA (6), AKT1 (1), IDH2 (1), JAK3 (1), and RET (1).

The number of Applicable M in each patient:

<table>
<thead>
<tr>
<th>Number of Mutations</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>30 (20%)</td>
</tr>
<tr>
<td>1</td>
<td>38 (27%)</td>
</tr>
<tr>
<td>2</td>
<td>30 (20%)</td>
</tr>
<tr>
<td>3</td>
<td>10 (7%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>5</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

DNA insufficient/canceled: 3 patients (3%).

Impact of NGS Testing:

- New therapy started (3%)
- Declined off-label treatment option (1%)
- No actionable/Applicable information (26%)
- Stable on current therapy (58%)
- Transitioned to hospice (7%)
- Lack of evidence to change the treatment plan (36%)
- Off-label access and insurance coverage (68%)

**CONCLUSIONS**

- Primary CNST demonstrate a significant number of applicable mutations (77% of patients) associated with sensitivity to targeted inhibitors along the PI3K, AKT, EGFR, CDK, IDH1 and BRAF pathways amongst others. The majority of patients (65%) had 1-2 potentially applicable mutations with a range of 0-5 across all patients.

- NGS may provide an opportunity to individualize treatment approaches and matching to clinical trial therapies, however access to such therapies remains a barrier.

- CNST represent a unique opportunity for investigation of targeted therapies and determination of efficacy of targeted approaches in CNST.

- A Precision Medicine Platform/Database is being utilized to integrate large-scale genomic and clinical information across a multi-hospital system as part of the PMRP to aid in cancer research and matching to clinical trial therapies. An expanded 300-gene alteration panel is pending.

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