GE-04. COMPREHENSIVE GENOMIC PROFILING (CGP) OF PEDIATRIC GLIOMAS REVEALS A HIGH FREQUENCY OF CLINICALLY RELEVANT GENOMIC ALTERATIONS (CRGA) ASSOCIATED WITH BENEFIT FROM TARGETED THERAPY

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BACKGROUND: Primary CNS tumors, which include both low-grade and high-grade gliomas, are the most common pediatric solid malignancies. We queried whether CGP could uncover a significant frequency of CRGA that could inform treatment decisions and improve clinical outcome for these aggressive tumors.

METHODS: DNA was extracted from 75 pediatric glioma formalin-fixed paraffin-embedded clinical specimens. Hybridization captured libraries of 236 (FoundationOne, n = 43) or 405 (FoundationOne Heme, n = 32) genes, plus select introns frequently rearranged in cancer were sequenced to high (>500x), uniform coverage. All classes of genomic alterations including base substitutions, small insertions and deletions, rearrangements, and copy number alterations, were evaluated and reported. CRGA were defined as GA associated with FDA approved therapies or targeted therapies in mechanism-driven clinical trials.

RESULTS: The median age of the patients was 9 years (range 0 to 18 years). There were 41 male (57%) and 34 female (43%) patients. The study included glioblastomas (n = 30, 42%), astrocytomas not otherwise specified (NOS) (n = 17, 24%), gliomas NOS (n = 10, 14%), pilocytic astrocytomas and anaplastic astrocytomas (9 each, 13%). 89% of cases harbored at least one CRGA. Pediatric gliomas frequently harbored short variants or copy number alterations in TP53 (39%); BRAF (15%) for which 82% were the V600E base substitution; CDKN2A/B (15%), NF1 (14%), PIK3CA (14%), ATRX (13%) and EGFR (11%). Ten cases (14%) harbored a BRAF fusion, including 44% of pilocytic astrocytomas. BRAF fusions included the known KIAA1549-BRAF and the novel CCDC6-BRAF and BCAS1-BRAF. ATG7-RAF1, ALK-PPCB1 and QK1-RAF1 rearrangements were also identified. Outcomes from cases where targeted therapy was utilized will be presented.

CONCLUSIONS: CRGA are frequently identified in pediatric glial tumors of both low-grade and high-grade histology and can be identified by CGP in the course of clinical care. CGP has the potential to identify opportunities for targeted therapies or enrollment in clinical trials for these patients.