ABSTRACT CITATION ID: NOAD179.0351
CTNI-69. REAL-TIME DRUG SCREENING AND GENOMIC TESTING TO DETERMINE INDIVIDUALIZED TREATMENT PLANS IN CHILDREN AND YOUNG ADULTS WITH RELAPSED MEDULLOBLASTOMA: PRELIMINARY REPORT OF PNOC027
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While current upfront multi-modal treatment for medulloblastoma is effective in many cases, for patients who relapse or don’t respond to initial therapy, effective treatment options are limited and novel therapeutic approaches are needed. The Pacific Pediatric Neuro-Oncology Consortium (PNOC) PNOC027 clinical trial investigates a precision medicine approach that combines real-time drug screening with whole exome and RNA sequencing of fresh tumor tissue to inform individualized treatment recommendations for children and young adults with relapsed medulloblastoma. The primary endpoint is to determine the feasibility of incorporating real-time drug screening with DNA/RNA sequencing of tumor to develop a treatment regimen of up to 4-drug of FDA approved agents within 21 business days of tumor acquisition. To this end, freshly isolated cells from relapsed medulloblastoma tumor tissue undergo high-throughput drug screening using a platform of 232 clinically available compounds in parallel with multi-omic genomic analyses to predict individualized tumor response to treatment. Drug responses are assessed after 72 hours of drug exposure and the results yield drug prioritizations based on cytotoxicity and predicted blood-brain barrier permeability. Drugs from different classes are selected based on results from drug screening and molecular analyses combined with patient age, prior treatments, and other medical conditions. Four patients have been enrolled to date and viable tissue samples have been successfully collected and analyzed with treatment recommendations rendered within 21 business days for all patients. The five drug classes with the highest in vitro responses on the drug screen are HDAC inhibitors, proteosome inhibitors, anthracyclines, DNA crosslinkers and kinase inhibitors. PNOC027 demonstrates preliminary feasibility of real-time drug screening combined with DNA/RNA sequencing to inform targeted therapy selection for patients with relapsed medulloblastoma in clinically relevant timeframes. The trial is informing an expanded precision-based approach for relapsed medulloblastoma and the impact of genetic and epigenetic alterations on treatment response.