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Precision Sequencing Algorithm in Pediatric Neurosurgery

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Introduction

Extreme tumor heterogeneity combined with dismal a prognosis for inoperable and recurrent tumors within pediatric neuro-oncology, has challenged us to think beyond current standards of care. Advanced sequencing (NGS) platforms are now commonly employed to identify clinically relevant targets to augment the current options. Our goal was to review or successes and identify an algorithm to simplify sequencing options, tailored to specific pathology.

Methods

Resected tumor tissue and blood from a histologically diverse patient cohort (n=70) was allocated for next generation sequencing(NGS) platforms including whole exome sequencing (WES), RNA sequencing, and methylation profiling. If no clinically actionable alterations were found with WES, deeper sequencing was performed at the gene expression level through RNA sequencing and fusion analyses. Methyl capture (RRBS) was utilized to delineate the epigenetic landscape for tumors such as recurrent ependymomas, high-grade gliomas, DIPG and gliomatosis cerebri (GC).

Results

20% of somatic alterations detected from WES demonstrated clinical utility which included the definition of a targetable mutation. Helping define a specific diagnosis,aiding a clinical team in providing prognosis information to a family, or facilitating an N of 1 clinical trial with a patient with recurrent or inoperable CNS disease was considered successful.

Conclusions

We present a streamlined and personalized sequencing approach to enhance our ability to eliminate indecision over competing sequencing platforms based on tumor location and frozen pathology. These platforms allows for interrogation of 20,000 genes and offers a unique data set relevant to known cancer specific somatic alterations and lesser known alterations that require further elucidation. Our personalized approach hopes to deliver actionable, diagnostic and clinically relevant information to treating neuro-oncology teams at a reasonable cost and speed, but significant challenges remain to widespread implementation.

Learning Objectives

1.To demonstrate the clinical utility of molecular profiling for pediatric CNS tumors

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