Molecular profiling of 267 pediatric cancers to identify potential clinically relevant targets

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Abstract #10037

Background: Even though only 1% of cancers occur in children, cancer is the leading killer of children. Many of the rare cancer types in children, the majority of which arise from the central nervous system, bone, or neuroblastoma. Methods: 267 cases referred to Caris Life Sciences were tested per physician request, including sequencing (Sanger, next generation [NGS]), protein expression (immunohistochemistry [IHC]), gene amplification (ISH or FISH), and/or MSMT validation. Diagnosis were collected from referring physicians at intake; for this analysis, cases were initially grouped into carcinomas (CA), sarcomas (SA), CNS, and carcinoma (CA).

Results, Molecular Profile

Table 1. Specific biomarker protein expression for all cases, by IHC, and broken out by the 3 most frequently seen subtypes, sarcoma (SA), CNS, and carcinoma (CA).

Figure 1. Distribution of CNS subtypes. The median age was 12.5 and the gender distribution was 56% female, 44% male.

Results, Pediatric CNS Patients

Figure 2. Biomarker alteration frequencies for each subtype. Ganglioglioma and ‘other’ not shown. A different profile was seen with the other gliomas and, one of the ‘other’ had a BAA mutation.

Figure 3. Distribution of sarcoma subtypes. The median age was 12 and the gender distribution was 47% female, 53% male.

Figure 4. Biomarker alteration frequencies for each subtype.

Table 3. Examples of guided therapy recommendations based on multi-platform molecular profiling.

Conclusions

- Molecular profiling using a multi-platform approach provides more actionable results; 83% more cases had actionable recommendations when also evaluated for protein expression and gene copy number.
- The addition of molecular profiling to help guide therapeutic decisions beyond the organs of origin could be of high value in pediatric cancers, as most drugs are restricted for pediatric patients.
- Using a rational approach based on biomarker status to identify clinical trials and off-label options in relapsed pediatric cancer patients may increase survival and may be a useful tool for tumor boards. Pediatric clinical trials would be enhanced with the use of biomarker status in inclusion/exclusion criteria, especially for targeted therapies, based on MCR guidelines for other cancer types.
- PD-1 and PD-L1 overexpression was not seen in 25 of 25 neuroblastomas evaluated, indicating that PD-1 and PD-L1-directed immunotherapy may not benefit these patients.
- High BCRP, MRPI and P-gp in pediatric carcinomas suggest resistance to chemotherapies.

References