10035 **Poster Session**

Comprehensive genomic profiling and individual therapeutic planning in high-risk/ refractory pediatric solid tumors: A single-center real-world study.

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Background: Despite major improvements in the survival of pediatric cancer patients that were achieved through the intensification of chemotherapy and the perfection of supportive care in the past decades, treatment outcomes for high-risk, relapsed, and refractory solid cancers remain unsatisfactory. Accelerating the progress of pediatric oncology requires both therapeutic advances and attention to reducing the long-term cytotoxic treatment-related side effects. This could be achieved by targeting specific molecular changes that drive pediatric malignancies. **Methods:** From September 2016 to August 2020, a total of 192 patients with pediatric high-risk solid tumors successfully underwent comprehensive genomic profiling. Since more than thirty patients had two or more biopsies from recurrent relapses, the total number of samples examined was 295. In the cohort, there were 78 cases of central nervous system tumors, 68 sarcomas, 14 neuroblastomas, 10 lymphomas, and 22 tumors of other histology. Whole-exome sequencing was performed in all patients, fusion gene analysis in 96% of patients, whole-transcriptome profiling in 84% of patients, and CNV analysis in 63% of patients. **Results:** The diagnostic yield of therapeutically actionable findings was 40%, with single-nucleotide variants and small insertions/deletions being the most common actionable alteration types. In 23% of patients, a clinically relevant gene fusion was identified. The majority of the identified fusions were of diagnostic significance, and 18% of those were therapeutically targetable gene fusions involving BRAF, RAF1, ALK, FGFR1, or NTRK2. Four patients were eligible for immunotherapy based on high tumor mutational burden ($>$ 10 mut/Mb). Lymphomas and CNS tumors showed the highest rate of patients with therapeutically actionable findings (60% and 56%, respectively), followed by neuroblastomas (36%), sarcomas (25%), and other solid tumors (23%). All results and individual treatment plans were discussed and approved at multidisciplinary molecular tumor boards. **Conclusions:** Precision medicine in pediatric oncology has rapidly developed over the last decade and resulted in new therapeutic options based on molecular biomarkers and increased our understanding of the complexity of pediatric malignancies. Supported by the Ministry of Health of the Czech Republic, grant nr. NU20-03-00240 and the project National Institute for Cancer Research (Programme EXCELES, ID Project No. LX22NPO5102) - Funded by the European Union - Next Generation EU. Research Sponsor: Czech Government.