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Congress Abstract

Molecular Profile of Extracranial Solid Tumors in Children: Diagnostic and Therapeutic Opportunities

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Introduction: Despite the relatively low mutational burden of most pediatric tumors, molecular genetic studies are increasingly being used in pediatric oncology. They enable confirmation of diagnosis, assessment of prognosis, and identification of potential targets for molecularly targeted therapy. Analysis of molecular diagnostic results in real-world clinical practice allows us to assess the capabilities and limitations of molecular diagnostics across different pediatric tumors.

Materials and Methods: Targeted sequencing of tumor DNA using a customized QIAseq panel (Qiagen, Germany) was performed in 334 patients with extracranial solid tumors treated at the Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology between 2018 and 2023.

Results: The highest diagnostic yield was observed in malignant rhabdoid tumors (n=23): diagnostically significant alterations were identified in 91.3% of patients.

In most cases, these alterations were highly specific to this tumor type and could be used to confirm the diagnosis alongside morphological and immunohistochemical data.

Prognostically significant molecular alterations were most frequently detected in neuroblastoma – in 66.7% of patients (112/168). The majority of these consisted of mutations in genes of the RAS/p53 signaling pathways, allowing further characterization of tumor biology and identification of patients with molecular features potentially associated with disease course and response to therapy.

Potentially therapeutically significant alterations were identified in 36% of patients (120/334). However, the presence of a molecular target did not always lead to the administration of the corresponding drug, as evidence for the efficacy of targeted therapy in children remains limited for a significant proportion of these alterations.

Targeted therapy based on molecular genetic testing results was administered in 6.3% of cases (21/334), predominantly in neuroblastoma (n=13).

It was used in the first-line setting or at first relapse in 66.7% of cases (14/21). In 61.9% (13/21) of patients, targeted agents were used in combination with standard antitumor therapy.

An objective response or disease stabilization lasting more than 6 months was observed in 66.7% (14/21) of patients. The median time to best response or stabilization was 6 months (range 0.8–12.3). The median duration of targeted therapy as monotherapy was 10.9 months (range 0.8–43.5), and in combination with chemotherapy – 12.3 months (range 0.3–61.5). In 42.8% (9/21) of patients, the response was maintained at the time of last follow-up.

Conclusion: Thus, molecular genetic plays an important role in improving the diagnosis and treatment of pediatric tumors. Futher accumulation of clinical and

molecular data will provide a deeper understanding of tumor biology and expand opportunities of personalized treatment.

Keywords: Personalized Medicine; Targeted Therapy; NGS; Pediatric Tumors; Neuroblastoma