Large Scale Precision Medicine Approach Successfully Applied to Pediatric Cancers With Poor Prognosis

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For immediate release
May 28, 2020

ASCO Perspective

“This study shows the potential of precision medicine to extend survival for our most precious population of patients with cancer, children. In our list of Research Priorities to Accelerate Progress, ASCO noted the importance of moving precision medicine into the care of pediatric patients. These early results provide the basis for continued research into this area,” said Chief Medical Officer and Executive Vice President Richard L. Schilsky, MD, FACP, FSCT, FASCO.

ALEXANDRIA, Va. — Researchers have developed an algorithm to identify molecular targets and pair them with targeted therapies for relapsed pediatric cancers with a poor prognosis. In a recent study, this approach extended the time until disease progression by three months for a small group of pediatric patients with very high-priority targets. The study findings will be presented during the virtual scientific program of the 2020 American Society of Clinical Oncology (ASCO) Annual Meeting.

Study at a Glance

| Focus | Test algorithm to identify molecular targets and pair them with targeted therapies for relapsed pediatric cancers with a poor prognosis |
Population

525 pediatric patients from the INFORM registry

Findings

8% of patients had a very high-priority treatment target; of 20 matched with targeted therapy, median progression-free survival of 204.5 days

Significance

Demonstrates feasibility of precision medicine in children with rare cancers with poor prognosis

While current treatment of childhood cancers results in high overall cure rates, relapsed high-risk disease is associated with a poor prognosis. For the most part, precision oncology has yet to be applied in pediatric cancer care, unlike in adult cancer where it has improved outcomes.

“For pediatric patients, if the cancer has relapsed, the prognosis is poor and there are few new innovative treatments,” said lead author Cornelis van Tilburg, MD, PhD, a pediatric oncologist at Hopp Children’s Cancer Center Heidelberg. “Compare this to adult oncology, where there are many new trials, many new biomarkers, and many new drugs. Pediatric oncology is really lagging behind when it comes to precision medicine and the development of new drugs.”

The INdividualized Therapy FOr Relapsed Malignancies in Childhood, or INFORM, registry was developed by a consortium of pediatric oncologists and genomics researchers to develop precision medicine-based approaches and to assess their efficacy across high-risk relapsed or therapy refractory pediatric cancers.

Key Findings

When grouped by the highest priority target for each patient — ranging from molecular alterations to changes in gene expression in molecular pathways important to cancer development and survival — 8% of patients had a very high-priority level target, followed by high (14.8%), moderate (20.3%), intermediate (23.6%), borderline (14.4%), low (2.5%), and very
low (1%) priority, and no actionable target (15.4%).

In all, 149 patients received targeted treatment based on the targets identified using the algorithm at the discretion of their clinical pediatric oncologist. Of these, 20 had a very high-priority level target – mainly **ALK**, **BRAF**, and **NRAS** mutations and **MET** and **NTRK**-fusions. Patients in this group had a median progression-free survival of 204.5 days compared to 114 days for all other patients. There were no clinically relevant differences in overall survival.

The findings show that it is possible to identify precision targets in relapsed pediatric cancers that can guide clinical decision making about treatment approaches.

“This registry has opened up the genomic landscape in pediatric oncology,” said Dr. van Tilburg. “It provides a unique source of information to help match new drugs or drug ideas with suitable biomarkers in certain pediatric patient populations,” he said.

**About the Study**

The INFORM registry involves the collection of clinical and molecular data from fresh-frozen tumor material of pediatric patients with refractory/relapsed/progressive malignant disease. This analysis includes 525 patients from eight countries with a median age of 12 years.

The 7-step algorithm prioritized molecular alterations or affected pathways, which would theoretically be targetable by an approved drug or an investigational agent. The priority levels were based on characteristics such as druggability, genetic change/expression, and direct drug target/pathway activation. Using the algorithm, the researchers identified subgroups of patients with genomic or molecular characteristics ranging from highest priority for pairing with a targeted drug to no actionable target. Treating oncologists had access to and could use the molecular target information for clinical decision making. In addition, INFORM provided important diagnostic information like underlying cancer predisposition syndromes and diagnostic refinements in brain tumors.

**Next Steps**

The researchers plan to continue to analyze data from the registry using the algorithm.
Additional molecular and functional analyses are being implemented for the registry, including ex vivo drug screens on viable tumor material and complex biomarker algorithms. In addition, based on the results obtained from the INFORM registry, a series of biomarker-driven phase I/II trials (called INFORM2) has been launched.

**Funding**
The study was funded by German Cancer Aid, German Childhood Cancer Foundation, Ein Herz für Kinder Foundation, and German Cancer Consortium.

**For your readers:**
What Is Personalized Cancer Medicine?
Childhood Cancer

**View the disclosures for the 2020 Cancer Communications Committee:**

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**ATTRIBUTION TO THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY ANNUAL MEETING IS REQUESTED IN ALL COVERAGE.**

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**View the abstract**
Watch the 7-minute press briefing presentation

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