

First successful treatment of pediatric high-risk refractory neuroblastoma with PARP inhibition

August 15 2024



Credit: Anna Shvets from Pexels

St. Jude Children's Research Hospital scientists report the first successful treatment of a pediatric patient with high-risk refractory

neuroblastoma using a targeted therapy guided by clinical genomics.

Poly (ADP-ribose) polymerase (PARP) inhibition successfully exploited an identified genetic vulnerability in the patient's cancer. The vulnerability was a mutation in the BARD1 gene, causing a defect in a DNA damage repair pathway.

PARP inhibition, in combination with chemotherapeutics, exploited the cancer's DNA damage repair defect, eventually leading to the malignancy's destruction. The report is [published](#) in the *New England Journal of Medicine*.

"At the time the patient came to St. Jude, multiple therapies had failed them," said co-corresponding author Sara Federico, MD, St. Jude Department of Oncology, Division of Solid Tumor director.

"Once we identified their specific BARD1 mutation, we were able to give them [targeted therapy](#) and eradicate their cancer. We were thrilled to see a dramatic clinical response. The patient has been off therapy for more than two years now. This [treatment regimen](#) may be successfully used for other patients with BARD1 mutations in the future."

Refractory neuroblastoma, which resists frontline conventional treatment, is a high-risk disease with a poor prognosis. The St. Jude team used germline DNA and RNA sequencing to look for new vulnerabilities in the patient's cancer that could be targeted therapeutically. Analyzing the data led to identifying BARD1 as driver mutation in this patient's cancer.

"Understanding the genetic basis of an individual cancer, in this patient the complete loss of BARD1 in the tumor, led to the impressive clinical outcomes observed after PARP inhibition," said co-corresponding author Jinghui Zhang, Ph.D., Endowed Chair of Bioinformatics, St. Jude

Department of Computational Biology.

"This case report demonstrates the potential impact of multi-omics analysis of RNA and DNA in the clinical setting. Such computational analysis is critical to assess target vulnerability and pediatric patient eligibility for precision treatments such as PARP inhibition."

After uncovering BARD1's involvement, the oncologists adapted treatment to PARP inhibitor talazoparib in combination with irinotecan. Talazoparib is already Food and Drug Administration approved for use in different indications adults.

The pediatric patient has been off therapy for over two and a half years with no detectable disease, making this the first report of a neuroblastoma patient with a BARD1 mutation successfully treated with PARP inhibition. This provides rationale for future treatments to target vulnerabilities in DNA damage response genes in solid tumors.

More information: Margaret Cupit-Link et al, Response to PARP Inhibition in BARD1 -Mutated Refractory Neuroblastoma, *New England Journal of Medicine* (2024). [DOI: 10.1056/NEJMc2403316](https://doi.org/10.1056/NEJMc2403316)

Provided by St. Jude Children's Research Hospital

Citation: First successful treatment of pediatric high-risk refractory neuroblastoma with PARP inhibition (2024, August 15) retrieved 15 August 2024 from <https://medicalxpress.com/news/2024-08-successful-treatment-pediatric-high-refractory.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.