

# Isle Kids Will Try Targeted Therapy (Star-Advertiser)

Originally published in the Star-Advertiser.

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## A trial program at Kapiolani will zero in on the genetic makeup of a tumor, then tailor a remedy for the child

Children in Hawaii with stubborn cancers that resist conventional treatment will soon have a chance to try a groundbreaking approach that matches medicines to the molecular makeup and mutations of their individual tumors. Kapiolani Medical Center for Women & Children is one of 15 hospitals taking part in the nation's only pediatric cancer trial using molecularly targeted therapy. A new phase of the trial starts next month.

“For the first time in pediatrics, we have the potential to treat tumors not just for how they look, but how they are under the hood, at the very level of their genes,” said Dr. Randal Wada, principal investigator in the study at Kapiolani and an associate professor at the University of Hawaii Nancy Atmospera-Walch School of Nursing. “This represents a start of a way to look at tumors in a different light and ask the question, ‘How do they operate mechanistically?’ and to design therapy that way.” The trial, the first of its kind, is aimed at children with otherwise incurable cancers.



Samples of their tumors will be sent to the Translational Genomics Research Institute, in Phoenix, for analysis. Dell supercomputers will scrutinize the genetic information and help pinpoint effective treatments from a wide-ranging medicine cabinet, including naturopathic remedies. Children in Hawaii whose tumors have outwitted regular therapy may be eligible for the trial, which is approved by the Food and Drug Administration. Up to 50 patients across the country will be enrolled in the study, formally known as "Molecular Guided Therapy for the Treatment of Patients with Relapsed and Refractory Childhood Cancers."

Just a handful of children living in Hawaii are expected to qualify for the trial over the next year because most pediatric cancers are cured with regular therapy, said Wada, who heads the pediatric hematology/oncology division at Kapiolani. Other kids who are willing to come to Hawaii for treatment may also be eligible. "We are focusing on the patients that have not responded to standard therapy, the very difficult cases, where really we don't know what else to do," said Dr. Giselle Sholler, the trial's principal investigator and director of the Innovative Therapeutics Clinic at Helen DeVos Children's Hospital in Grand Rapids, Mich.

Typically in drug trials, one experimental medicine is used on a large, randomized sample of patients under carefully controlled conditions. This study turns that formula around, diving deep into each person's disease to identify the specific mutations and genetic pathways activated in each cancer, and then choosing the therapy. That's because cancer is a wily and resourceful adversary that can manifest in myriad ways. "Many people will think of lung cancer as a single thing, when actually it is multiple different specific entities," Wada said. "Even cancers that look the same under the microscope can be very different genetically." "And even more fascinating," he added, "cancers that look differently under the microscope, a liver cancer or a kidney cancer for

example, could have very similar genetic defects.”

The trial rests on the power of computing, with therapies based on a massive input of genetic information. An earlier phase of the trial used “gene chips,” or tiny integrated circuits, to answer tens of thousands of questions at once. The new phase reaches far beyond that. “The previous study used ‘chips’ that are arrays capable of screening 80 (thousand) to 100,000 gene regions at a time,” Wada said. “But the new version will directly sequence the whole genome worth of both DNA and RNA, essentially measuring every single bit of every single gene and every single RNA molecule in the cell.”

Dell’s supercomputing technology provides the backbone for the study. The computer giant also gave \$1.6 million last year and \$1.5 million this year to the Neuroblastoma and Medulloblastoma Translational Research Consortium at Helen DeVos Hospital to run the trial. “It is really because of Dell that we have been able to go deeper and deeper,” Sholler said. “Really crunching that data is an incredibly powerful feat.” “It used to take two months, then one month, and now they have shortened it to two weeks,” she said. “It’s mind-blowing what they have been able to do, with the amount of genetic data that comes out of each patient. We look at 300 different medications and the pathways they target.”

A board including oncologists, bioinformaticians, pharmacists and a naturopathic physician will assess the recommended options and come up with personal solutions of up to four medications for each patient. As the children are treated, researchers will continue studying viable parts of their tumors in the laboratory. “A portion of the sample also comes to my lab where the cells are grown in culture, and we’re able to then do further testing to help validate our predictions,” Sholler said. “In the patient we can only choose a couple of medicines to use; in the lab we can screen that tumor cell with very many different medications.”

Just one patient in Hawaii participated in an earlier version of the trial. He suffered from Ewing's sarcoma, a rare bone cancer that was growing in his leg and had spread to his lungs. The menu of drugs prescribed through the trial included chemotherapy and two remedies not normally prescribed for cancer: an antibiotic and a cough medicine. His physician, Dr. Darryl Glaser, a pediatric hematologist oncologist at Kapiolani, said the therapy appeared to help.

"He seemed to respond to the medicines," Glaser said. "I believe they gave him more time. But his cancer was so advanced that he eventually succumbed to complications of the disease." With a trial geared toward the sickest patients, progress is measured in small steps. The hope is that molecularly targeted therapy will enhance a patient's quality of life by focusing the line of attack. "Eighty percent of childhood cancer is cured with a regular therapy, so most of our patients will never have to consider this type of trial," said Glaser, who is also an assistant professor at the UH School of Medicine. "The patients we are talking about are those who are very sick, who have exhausted other kinds of therapy.

"As a treating physician, it is very comforting for me to know that for that small minority of patients whose cancers relapse, I'll have a chance to offer them therapy that's targeted to their specific tumor." "It gives another opportunity to children who may have no more options left," he said. "Personalized treatment offers much more chance of success."