Old drug with a new purpose may offer hope for children with neuroblastoma

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A new Phase I clinical trial sponsored by the Vermont Cancer Center at the University of Vermont and Fletcher Allen Health Care has opened to test the investigational drug DFMO, or alpha-difluoromethylornithine, as a treatment for the pediatric cancer neuroblastoma. According to researchers at the Cancer Research Center at the University of Hawaii, and the Vermont Cancer Center , the study will monitor the safety of DFMO usage among neuroblastoma patients and test whether the drug is effective in reducing or eradicating neuroblastoma tumor cells.

Each year, approximately 650 children in the United States are diagnosed with neuroblastoma, a rare form of cancer that occurs when malignant cells form in the sympathetic nervous system, which may arise in the adrenal gland, neck, chest or abdomen. It is usually diagnosed in children less than 6 years of age. While many infants less than a year old may experience complete regression of primary tumors, older children are often confronted with metastatic neuroblastoma that is aggressive and responds poorly to even the most intense multi-component drug regimens.

DFMO is a proven therapy for Trypanosomiasis or "African Sleeping Sickness." Discovered in the 1970's, the drug was approved by the FDA and demonstrated few side effects in patient usage. In recent years, it has attracted renewed interest from researchers as a possible treatment for certain cancers.

One of the first to study DFMO in relation to neuroblastoma was André

Bachmann, PhD, MS, and associate professor at the University of Hawaii's Cancer Research Center. In 2002, Bachmann began testing DFMO's effect on neuroblastoma cells in vitro. Results were encouraging enough to secure National Cancer Institute funding in 2006. Bachmann teamed up with Giselle Sholler, M.D., a pediatric oncologist and researcher at the Vermont Cancer at the University of Vermont and Vermont Children's Hospital at Fletcher Allen Health Care, and they later demonstrated evidence of the drug's ability to cure neuroblastoma cancers in mice by inhibiting an enzyme implicated in aggressive tumor development.

DFMO is an inhibitor that specifically targets a key protein called ornithine decarboxylase (ODC). This protein makes the polyamine molecules. Both ODC and polyamines are often accumulated in cancer and contribute to tumor growth.

"While this has been known for years, I was surprised to find (in 2002) that DFMO had never seriously been considered for the treatment of neuroblastoma, a MYCN-driven cancer," said Bachmann. "Since MYCN activates ODC, I felt immediately that there was a good chance that DFMO could be effective in this particular cancer. I was also encouraged because the drug had been used in patients with African Sleeping Sickness, has low toxicity, and is water soluble allowing oral intake, a great advantage for pediatric patients," he added.

Bachmann and Sholler have continued this research collaboration in moving the laboratory findings to an actual drug trial. Sholler is the principal investigator of the clinical study and worked with Bachmann to co-write the protocol, which uses DFMO alone and in combination with a second drug, etoposide.

"DFMO is a very promising drug in that it targets an enzyme important in neuroblastoma growth," said Sholler. "It's very exciting to have this

oral option available for children with relapsed neuroblastoma who have had aggressive previous therapy and are unable to tolerate further chemotherapies. Based on adult cancer studies, we expect this drug to be well tolerated with minimal side effects. We are hopeful that this trial will show response as well as improving quality of life for children living with this disease allowing them to spend less time at the hospital and more with their families.

Provided by University of Hawaii at Manoa