SOUTHWESTERN NEWS

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NEW CLINICAL TRIALS TO BEGIN ON OLD DRUG THAT MAY HELP CHILDREN WITH LEUKEMIA

DALLAS — March 11, 1996 — Pediatric cancer specialists at UT Southwestern Medical Center at Dallas plan to bring an old cancer-fighter off the bench and test its effectiveness in a new generation of children with leukemia.

Dr. Barton Kamen, professor of pediatrics and pharmacology, and his colleagues believe aminopterin (AMT), one of the first chemotherapy drugs used to treat children with acute lymphoblastic leukemia, shows promise as an alternative for some children who cannot be successfully treated with the standard chemotherapy drug, methotrexate (MTX). The researchers published their findings in a recent issue of *Clinical Cancer Research*.

They are currently enrolling patients in clinical trials to test AMT.

"We've known for 45 years that aminopterin was a good drug, but because of concerns about toxicity, physicians stopped using it and turned to methotrexate," Kamen explained. "We've also learned, however, that methotrexate isn't a good choice for all leukemia patients, so we keep looking for treatment alternatives."

Acute lymphoblastic leukemia is the most common form of childhood cancer; about 25 percent of all children diagnosed with cancer have this form. About 70 percent of these patients are effectively treated and remain disease-free. Kamen's latest research suggests AMT may push that success rate even higher.

"Some children's disease is not controlled by methotrexate so they relapse," Kamen said. "By studying how methotrexate is metabolized in the body we began to see why these children weren't treated successfully. That opened the door once again to explore the use of aminopterin, which we know is more potent and more effectively metabolized than methotrexate."

Kamen explained that, as a physician treating children with acute lymphoblastic leukemia, he has grown increasingly frustrated with the lack of new, effective drugs. That

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frustration prompted his experiments with AMT. He said it has been necessary to locate a new manufacturer to supply AMT for the trials. "During 40 years of use, methotrexate basically moved it off the shelf."

Kamen, holder of the Carl B. and Florence E. King Foundation Distinguished Chair in Pediatric Oncology Research and an American Cancer Society Clinical Research Professor, compared AMT with MTX in laboratory tests using cells from children with leukemia. The researchers found AMT was metabolized more completely by the cells than MTX, which explains some of the problems patients have with MTX.

Both AMT and MTX are antifolates — drugs that look like the folate vitamin, or folic acid, to a cell and usually interfere with its function. Folates are required for the growth of cells, and antifolates kill cells by interfering with their metabolism.

Kamen believes the early concerns about AMT can be addressed. "In 40 years at the bedside and bench, we've learned a great deal about drug-induced toxicity. We're better equipped to guard against it and treat it." He also expects that more advanced manufacturing methods should deliver a safer AMT product.

"Little progress has been made in finding and introducing new drugs into the cancer armamentarium, so it's not unreasonable to go back to an old drug and apply new knowledge in treating this generation of young cancer patients," Kamen said.

Call (214) 648-3896 for more information on the aminopterin clinical trial.

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