SOUTHWESTERN NEWS

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UT SOUTHWESTERN RECEIVES FDA GRANT TO CONTINUE STUDIES OF CANCER-FIGHTING DRUG NOT USED FOR PAST 50 YEARS

DALLAS – Oct. 16, 1997 – Success in treating stubborn cancers with a drug that was shelved 50 years ago has encouraged the Food and Drug Administration (FDA) to provide a three-year, $447,534 grant to UT Southwestern Medical Center at Dallas to begin second-stage clinical tests of the drug, aminopterin.

Aminopterin is the "parent" of the commonly prescribed, cancer-fighting drug methotrexate. Originally tested in the 1940s, it fell out of favor with doctors because of concerns about toxicity and difficulties synthesizing it. In recent years, Dr. Barton Kamen, a professor of pediatrics and pharmacology at UT Southwestern, has taken a new look at the drug to see if it might prove effective in treating patients – particularly children with leukemia – whose cancer does not respond to methotrexate.

The pediatrician doesn't usually treat adults, but Ingrid Cofield, a 49-year-old woman from Rowlett, Texas, is glad he made an exception.

Cofield was one of several adults Kamen enrolled in a Phase I trial of the drug aminopterin last year.

Phase I trials usually are conducted to see what doses of drugs patients can tolerate. But the aminopterin made a tumor in Cofield's liver disappear.

"I didn't expect this at all," Cofield said. "I thought maybe it would become a little smaller, but not that it would all go away."

Cofield originally was diagnosed with endometrial cancer in 1993. She had a hysterectomy to remove her cancerous uterus and then went through chemotherapy. The cancer was gone for a year, but then she discovered a lump in her groin. Hormonal therapy prevented enlargement for a while, but the lump started growing again. She again underwent chemotherapy, but tests soon showed the tumor had spread to her liver.

Dr. David Scott Miller, an associate professor of obstetrics and gynecology and holder

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of the Dallas Foundation Chair in Gynecologic Oncology at UT Southwestern, was Cofield's doctor. Knowing of Kamen's aminopterin trial, Miller referred her to Kamen, and Cofield was enrolled in the study.

"I've always been a fighter," said Cofield, who won the women's master's division of the 1988 and 1989 White Rock marathons. "They gave me a choice of going home and living what life I had left or trying the experimental treatment. I said, 'I'd try it.'"

Of the 20 patients who participated in the Phase I trial, three others also showed a positive response to the aminopterin: an 8-year-old boy with a nerve-sheath tumor, a 10-year-old boy with acute-myelogenous leukemia (AML) and a 4-year-old girl with a neuroectodermal tumor.

Kamen presented his findings to the American Society for Clinical Oncology (ASCO) in May.

"This is terrific news for the patients and terrific news for us," said Kamen, holder of the Carl B. and Florence E. King Foundation Distinguished Chair in Pediatric Oncology Research. "In the 20 years I've been doing this, I can't remember this many responses in a Phase I trial. This means we can be optimistic we have an effective drug."

The FDA-funded Phase II clinical trial of the drug is already under way. The first patient enrolled in the trial, which focuses on leukemia patients, is in complete remission.

Four other institutions are participating in the Phase II study: The University of Chicago Division of the Biological Sciences Pritzker School of Medicine, St. Jude Children's Research Hospital in Memphis, UT M.D. Anderson Cancer Center in Houston and UT Health Science Center at San Antonio.

Because of aminopterin's success in Cofield, doctors at UT Southwestern also are beginning a separate clinical trial of the drug on women with persistent or recurrent endometrial cancer.

Cofield, meanwhile, still cannot be considered cured, but Kamen said her complete remission means she is much more likely to be cancer-free in the future.

The aminopterin is made for UT Southwestern by ILEX Oncology of San Antonio.

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