Cancer drug first tested in pet dogs begins human trials

February 26 2015

A new anti-cancer compound, PAC-1, spurs cell death in cancer cells while sparing healthy cells. Credit: L. Brian Stauffer

A new drug that prompts cancer cells to self-destruct while sparing healthy cells is now entering phase I clinical trials in humans. The drug, called PAC-1, first showed promise in the treatment of pet dogs with spontaneously occurring cancers, and is still in clinical trials in dogs with

osteosarcoma.

The compound was discovered and is being developed based on the hypothesis that most cancers have elevated levels of an enzyme called procaspase-3," said University of Illinois chemistry professor Paul Hergenrother, who discovered the anti-cancer effects of PAC-1 more than a decade ago. "Procaspase-3 is an enzyme that, when turned on, kills cells."

Cancer cells, however, override this normal cell-recycling pathway, he said.

"Even though they have elevated levels of procaspase-3, cancer cells never turn the enzyme on. So they keep growing and become tumors," he said. "PAC-1 restores the activity of procaspase-3 and, because the enzyme is elevated in cancer cells, it targets cancer cells over non-cancerous cells."

Early tests of the drug's effectiveness came when Hergenrother collaborated with U. of I. veterinary clinical sciences professor Timothy Fan, who tested PAC-1 in his canine cancer patients. These clinical trials helped the researchers find the best way to deliver the drug - it is now in pill form for both human and canine patients - and led to new insights into the drug's activity and potential, Fan said.

"One of PAC-1's greatest strengths is that it synergizes with other drugs, increasing the anti-cancer effects of many compounds that are out there," Fan said. "It also crosses the blood-brain barrier very well," making it a good candidate for the treatment of brain cancer - in humans and dogs, he said.

"Treatment for brain cancer is a huge area of need," said Dr. Arkadiusz Dudek, a physician and professor of hematology and oncology at the

University of Illinois at Chicago, who will direct the human clinical trials at the U. of I. Cancer Center in Chicago. "Currently, we do not have that many therapies available for glioblastoma multiforme," the most common and malignant type of brain cancer.

PAC-1 is one of only a few drug agents developed and tested in animals and in humans at a single institution, Dudek said. The work in dogs led to the formation of the Illinois-based company Vanquish Oncolog to develop this anti-cancer agent. Vanquish received initial support from the investment firm IllinoisVENTURES, and an anonymous "angel investor" provided the funding to move the drug through preclinical trials and gain federal FDA approval to begin a phase I clinical trial.

The trial, led by Dr. Oana Danciu of the U. of I. Hospital and Health Sciences System in Chicago, opened enrollment this month to patients with advanced malignancies. Doctors will start the first patients at a low dose and gradually increase the dose and watch for side effects, the researchers said.

"Because this is the first time ever a human will take PAC-1, we will track the blood concentration of the compound over time at different doses," Hergenrother said. Once they find the optimal dose, clinicians will start new trials in brain cancer patients at the U. of I. Cancer Center and at Johns Hopkins University School of Medicine in Baltimore. (More information about the clinical trials is available here.)

In the meantime, Fan and his colleagues hope to begin clinical trials of PAC-1 in pet dogs with brain cancer. They will look at PAC-1 in combination with radiation and in combination with temozolomide, a key brain cancer drug used in humans and dogs.

The work in dogs will aid in understanding how human brain cancers may respond to the new treatment, Fan said.