Cancer drug tested in pet dogs is now bound for human trials

17 July 2013

Thanks to a new $2 million investment, a drug that spurs cancer cells to self-destruct while sparing healthy cells is on the road to human clinical trials. The compound, known as PAC-1, has so far proven safe and has promising anti-cancer effects in cell culture, in mouse models of cancer and in pet dogs with spontaneously occurring lymphomas and osteosarcomas.

If PAC-1 (pack one) makes it through the U.S. Food and Drug Administration's Investigational New Drug review, the first human (Phase I) clinical trial of the drug will begin in mid-2014. The investor, who wishes to remain anonymous, has an option to invest another $2 million to take the drug into human trials. The clinical work will be conducted at the University of Illinois Cancer Center in Chicago.

"The trial is going to be geared toward brain cancer patients," said U. of I. chemistry professor Paul Hergenrother, who discovered PAC-1's anti-cancer capabilities in 2006 and has been refining and testing it ever since. "One of the unusual features of this drug is that it does get into the brain, which most cancer drugs do not. So we want to embrace that and try to address the unmet clinical need of brain cancer."

The researchers noted that the compound is still in the early stages of development, and must pass toxicological tests in two species as well as other pharmacology toxicity testing before it can be tried in human subjects.

The new investment is the outgrowth of years of testing and development of PAC-1 and derivative compounds in dogs with naturally occurring cancers, said Illinois professor of veterinary clinical medicine Tim Fan, who coordinated clinical trials of the drug in canine patients at the U. of I. Veterinary Teaching Hospital.

"We know that mice will always be used as a traditional model for cancer research," Fan said. "But conventional preclinical models use mice with induced cancers, which fail to faithfully recapitulate the development of natural cancers. This means that novel therapeutics that may be effective in mice might fail in patients that develop cancer spontaneously, as observed in both dogs and people."

The researchers emphasized that the dogs used in the testing of PAC-1 were pets from the community with spontaneously occurring cancers, not laboratory animals with induced cancers.

"In addition to paving the way for the human trial, we have helped many veterinary patients that would not have otherwise received treatments for their cancer," Fan said.

PAC-1 targets a cellular enzyme, procaspase-3, that when activated spurs a series of reactions inside the cell that cause it to self-destruct, Hergenrother said. Procaspase-3 has long been an attractive target for cancer therapy, in part because cancers often interfere with normal cell death, and in part because many tumors—including those of the breast, colon, liver and lung, along with lymphoma and melanoma—contain high levels of procaspase-3.

"The target, procaspase-3 activation, and the extensive amount of in vitro and animal data that Dr. Hergenrother and Dr. Fan had generated are what attracted me to this project," said Ted Tarasow, the chief executive officer of Vanquish Oncology, a drug development startup company founded by Hergenrother and Tarasow in 2011.

"Procaspase-3 activation has long been recognized as a high potential target for oncology therapeutics, but largely has been met with frustration in terms of finding compounds that could actually influence its activity in vivo," Tarasow said. "And so the compounds that professor Hergenrother developed

and that Vanquish is pursuing are likely to be the first procaspase-3-activating agents to make it to the clinic despite a lot of interest and investment in this target over the years."

Vanquish Oncology "has exclusively licensed the technology from the University of Illinois and is focused on moving PAC-1 into the clinic," Tarasow said. "As with any investigational agent, determining the true safety and efficacy profile of PAC-1 will take several years of human clinical trials."

PAC-1 has other desirable attributes, said Arkadiusz Dudek, a physician and professor of hematology and oncology at the U. of I. at Chicago.

"What is interesting about Hergenrother's discovery is that it has a unique ability to penetrate to brain tumors," said Dudek, who will design and supervise the first PAC-1 clinical trial in humans at the U. of I. Cancer Center. "This is an area of interest for us. If successful, it will make a huge impact on survival, quality of life and disease control in patients with primary or metastatic brain tumors."

More information:
www.ncbi.nlm.nih.gov/pmc/articles/PMC3113694/

Provided by University of Illinois at Urbana-Champaign