New compound advances into Phase 1 trial for pancreatic cancer

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Erkki Ruoslahti, M.D., Ph.D., distinguished professor at SBP and founder, president and CEO of DrugCendR. Credit: John Gestaldo

A compound discovered at Sanford Burnham Prebys Medical Discovery Institute (SBP) has advanced into a Phase 1 trial for metastatic

pancreatic cancer. Called CEND-1 (scientifically known as iRGD), the compound was exclusively licensed in 2015 to a private company, DrugCendR Inc. The drug candidate was discovered in the laboratory of Erkki Ruoslahti, M.D., Ph.D., distinguished professor at SBP and founder, president and CEO of DrugCendR.

Solid tumors, such as pancreatic cancer, are difficult to treat. The tumor cells are often surrounded by thick fibrotic walls, making it hard for treatments to get access to the tumor cells. As a result, many solid tumors are also some of the deadliest cancers, including brain, ovarian and pancreatic cancer. Only 8.5 percent of people with pancreatic cancer live more than five years.

CEND-1 overcomes this barrier to allow cancer treatments to penetrate further into the tumor. The compound harnesses a transport pathway that appears to be designed to ferry nutrients to a tissue that is nutrient deficient. The SBP team named it the CendR pathway.

"Cancer cells hijack processes they can use to fuel tumor growth, and the CendR pathway is one such route," says Ruoslahti. "CEND-1 activates the CendR pathway only in tumors and not elsewhere in the body, and that allows us to sneak in a drug into the activated pathway."

Research in mouse models of cancer shows that if a drug is given at the same time as CEND-1, it is swept into the transport pathway and eventually engulfed by the tumor cells. As a result, the drug is able to bypass the tumor's barrier, travel deep into the tumor and poison it—leaving healthy tissues unaffected.

"While this initial study focuses on pancreatic cancer, mouse experiments show that it works for many different kinds of solid tumors—including breast, brain, lung and ovarian cancers and melanoma," says Ruoslahti. "We expect that CEND-1 will be used with the anti-cancer

drugs patients already receive. CEND-1 doesn't modify drugs—but it can streamline their deep penetration into tumors."

Adds Kristiina Vuori, M.D., Ph.D., president of SBP, "We are very excited that Dr. Ruoslahti's breakthrough research has entered clinical trials. Our scientists strive every day to make discoveries and advance science to create better treatment options for patients. This is a major accomplishment that offers the potential for novel and effective therapy for pancreatic cancer."

The trial, called CEND1-001, is an open-label, multi-center study. Patients will receive CEND-1 and the chemotherapy drugs Gemzar (gemcitabine) and Abraxane (nab-paclitaxel) intravenously. The study is designed to evaluate safety and ideal drug dosage in people with metastatic pancreatic adenocarcinoma. For more information about the clinical trial, visit clinicaltrials.gov and use the identifier NCT03517176.

CEND-1 is a peptide that homes to tumors through a multi-step process. First, CEND-1 binds to tumor-specific integrins, alpha V beta 3 and alpha V beta 5, through a three-amino-acid motif comprised of arginine, glycine and aspartic acid. The peptide is then cleaved; and that product binds to a second receptor, neuropilin-1, which activates the CendR pathway.

CEND-1 is covered by 28 patents and patent applications in the U.S. and additional countries. It has been used for targeted delivery of drugs to tumors in more than 100 publications.

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