

Clinical trial to test safety of drug targeting leukemia cells

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Researchers at the University of California, San Diego School of Medicine, in partnership with the California Institute for Regenerative Medicine (CIRM) and Celgene Corporation, a New Jersey-based biopharmaceutical company, have launched a phase 1 human clinical trial to assess the safety and efficacy of a novel monoclonal antibody for patients with chronic lymphocytic leukemia (CLL).

CLL is the most common form of blood cancer in adults, with more than 15,000 new cases diagnosed each year in the United States. The new antibody targets ROR1, a protein used by embryonic cells during early development that is also exploited by [cancer cells](#) to promote tumor growth and metastasis – the spreading of cancer throughout the body that is responsible for 90 percent of all cancer-related deaths.

ROR1 is not expressed by normal adult cells, making it a specific marker of cancer cells in general and cancer stem cells in particular. Because ROR1 is a primary driver of tumor growth and metastasis, researchers believe it presents an excellent target for anti-cancer therapy.

Developed at UC San Diego Moores Cancer Center by Thomas Kipps, MD, PhD, who holds the Evelyn and Edwin Tasch Chair in Cancer Research, and colleagues, the antibody is called cirmtuzumab (also known as UC-961). In previous animal studies, Kipps' team reported that ROR1 is singularly expressed on CLL and also on a variety of different cancers, including cancers of the breast, pancreas, colon, lung and ovary. In mouse models of CLL, ROR1 acts as an accelerant when combined with another oncogene to produce a faster-growing, more aggressive cancer.

Cirmtuzumab is based on a humanized anti-ROR1 monoclonal antibody that, in mouse studies, reduced levels of ROR1, impairing the growth and survival of CLL cells and making them more vulnerable to other [anti-cancer drugs](#).

Cirmtuzumab was developed under the auspices of the CIRM HALT leukemia grant awarded to Dennis Carson, MD, principal investigator, and Catriona Jamieson, MD, PhD, co-principal investigator to develop six distinct therapies against cancer stem cells. Kipps led one of the six projects to generate antibodies against ROR1, leading to the cirmtuzumab trial in patients with CLL.

"The primary goal of this phase I clinical trial is to evaluate whether cirmtuzumab is a safe and well-tolerated cancer stem cell-targeted agent in patients with CLL," said Jamieson, chief of the Division of Regenerative Medicine, associate professor of medicine, director of stem cell research at UC San Diego Moores Cancer Center, deputy director of the Sanford Stem Cell Clinical Center and the principal investigator of the cirmtuzumab clinical trial.

Michael Choi, MD, assistant clinical professor of medicine and co-principal investigator of the clinical trial, said, "The trial will involve 33 to 78 patients with relapsed or refractory CLL, who will receive an intravenous infusion every 14 days at Moores, followed by regular monitoring and clinic visits to assess efficacy and identify and manage any adverse effects. Initial treatment is planned for two months."

Kipps suggested that drugs like cirmtuzumab, if ultimately shown to be effective, could lead to a new type of anti-cancer therapy. "Every drug has limits. Usually anti-cancer drugs cannot cure cancer. Even after achieving a good response to anti-cancer drugs, the cancer can come back and spread to other parts of the body," he said.

"This is thought to be due to cancer [stem cells](#), which are relatively resistant to our current anti-cancer drugs. Because [cancer stem cells](#) may require ROR1 for their growth, survival and movement through the body, targeting ROR1 could be a way to eradicate the seeds of the cancer that

are responsible for metastasis or relapse after other forms of treatment.

"I see cirmtuzumab as perhaps also synergizing with other forms of treatment to provide for more effective anti-cancer therapies. It's the cocktail approach, similar to what's been shown to be effective in treating patients with HIV. Multiple drugs attack multiple targets of the cancer, each eliminating subsets of malignant cells. When combined with anti-ROR1 therapy, we might also block the recurrence of cancer after treatment."

Kipps noted that discoveries like ROR1 are causing scientists to think of cancer metastasis in a different way. "It's sort of like the tumor is replaying a song we last played during our earliest stages of embryonic development, when our cells 'metastasized' to different sites to create our various organs. By turning off ROR1, we might end that tune and get on with life without [cancer](#)."

Provided by University of California - San Diego

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