Can a drug developed for sickle cell anemia mitigate lung damage in patients with COVID-19?

May 13 2020

Credit: CC0 Public Domain

Scientists around the globe are working to identify approved and

investigational drugs that can be repurposed to treat COVID-19.

Senicapoc study to assess whether drug can prevent SARS and lung damage and reduce days spent on a ventilator. Senicapoc study to assess whether drug can prevent SARS and lung damage and reduce days spent on a ventilator.

UC Davis Health researchers provided one of those repurposed drugs, senicapoc, to launch a clinical trial at Aarhus University in Denmark. The study will assess whether the drug can mitigate lung damage in patients with COVID-19.

Senicapoc was developed as a treatment for sickle cell anemia. Although it was found safe in clinical trials, it did not reduce the number of sickle-cell crises and was shelved.

John Olichney, the clinical core director for the UC Davis Alzheimer's Disease Center, Heike Wulff, a professor of pharmacology, and other UC Davis researchers have been evaluating senicapoc as a potential treatment for stroke and Alzheimer's disease.

"In the Alzheimer's research field, it is becoming more evident that the immune system often results in excess inflammation and certain cytokines that can interfere with the synapse and its memory functions," Olichney said.

Animal studies from UC Davis published in 2019 showed senicapoc reduced neuroinflammation by suppressing microglia—cells responsible for immune response in the brain—and mitigated Alzheimer's disease-like deficits in mice. The compelling data from these studies led to grants from the Alzheimer's Association and the Alzheimer's Drug Discovery Foundation to make senicapoc and repurpose it for a Phase 2 clinical trial for early and mild Alzheimer's disease at UC Davis.

Last year, Olichney and Wulff had a Good Manufacturing Practice (GMP) facility in China manufacture senicapoc for the clinical trial. GMP facilities ensure products are consistently produced and controlled according to the highest quality standards. Producing GMP drugs can be very expensive.

"The price is not much different if you make one kilogram or 10 kilograms of a drug because the cost really is for the GMP. We made additional senicapoc knowing we might need it for something else or that we might expand our trials," Wulff said. "Right now we are glad that we are in a position where we can conduct our Alzheimer's disease study and also provide senicapoc to the University of Aarhus for the COVID-19 study."

Study will investigate whether senicapoc can prevent SARS

Ulf Simonsen, a professor and doctor of medical science, is leading the clinical trial at Aarhus University in Denmark.

Senicapoc binds to calcium-activated potassium channels involved in fluid secretion on the surface of the airway in the lungs. The drug also binds to potassium channels in macrophages and T-cells—cells involved in immune responses.

What Simonsen and his colleagues discovered was that this combination—blocking secretions and mitigating the immune system reaction—was able to inhibit the development of severe acute respiratory syndrome (SARS) and damage to the lungs.

The discovery was significant enough that Simonsen and his research colleagues together with Aarhus University patented the discovery.

As the COVID-19 pandemic began to spread around the world, Simonsen received a grant from the Danish government to launch the clinical trial. The study is investigating whether treatment with senicapoc can prevent SARS and the lung damage seen in COVID-19, reducing the need for a patient to be on a ventilator.

He reached out to Olichney and Wulff, whom he knew from conferences and their research, to assist in sourcing senicapoc for the COVID-19 trial.

"By using senicapoc, we don't treat the viral infection, but we prevent or slow the development of the disease that leads to severe damage to the lungs," Simonsen explained.

After reaching an agreement with Aarhus University, UC Davis arranged to have the senicapoc shipped to Denmark from the GMP facility in China, where it was being stored.

"It has surprised me how fast things can move globally with the attempt to combatting coronavirus and how supportive people are when you have an idea how to do it," Simonsen said. "We are very happy for all the help and support that we got from Professor Heike Wulff and Professor John Olichney, which will allow us to conduct a clinical trial in severely ill patients with COVID-19 infection."

The clinical trial in Denmark will evaluate 46 patients in intensive care with low blood oxygen saturation levels. Simonsen hopes to share the study results in a few months.

"When a person is infected with COVID-19, the worst-case scenario is that they will suffer severe lung disease that could lead to death," Simonsen said. "This is the situation where the need for treatment with a ventilator occurs. It's also here that we hope the senicapoc treatment can

make a difference—if only so that the patients require a shorter period on a ventilator."

Provided by UC Davis