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Taking on obesity

Novartis is developing an experimental drug for weight loss.

By Veronica Meade-Kelly | Feb 26, 2018

*Read an **important program update** below this story.*

As a cardiologist at the Veterans Affairs (VA) Medical Center in Boston, Will Chutkow treats patients who have served in the US military. Because these patients are predominantly male, drink and smoke at an above-average rate, and have had stressful jobs, they are in the high-risk group for heart disease. Many are also among the 38% of US adults who suffer from obesity – a major risk factor for chronic illnesses such as heart disease and diabetes.

“The patients who I see at the VA are also, as you might imagine, a conscientious group. They take responsibility for the situation they’re in with their health,” says Chutkow, who is also a researcher at the Novartis Institutes for BioMedical Research (NIBR). “But when we recommend weight loss, like most patients, they have a near-impossible time shedding the pounds.”

These patients and others struggling to lose unwanted pounds could one day benefit from an experimental weight loss drug called LIK066. Chutkow and colleagues are testing LIK066 in clinical trials at Novartis, and it has demonstrated the potential to help reduce weight in people with obesity.

Filling a treatment void

Beyond life-altering bariatric surgery that permanently reduces the size of the stomach, many people try the “eat less, exercise more” approach to weight loss, which often doesn’t work. With obesity rates rising worldwide, a drug that effectively induces weight loss would address a major unmet medical need – one that Chutkow and other clinicians are all too familiar with.

“When I deal with obesity, I feel ill-equipped,” he explains. “I focus on what I can fix, which are the cardiovascular conditions that bring patients to my office. But I know that’s just the tip of the iceberg. There’s this underlying condition – obesity – that I’m not addressing, but I don’t have the tools I need.”

Results from a small, early-stage clinical trial of LIK066 could be a step in the right direction. They showed that patients who took the compound lost 6% more body weight over 12 weeks than those who took a placebo pill.

Will Chutkow called on researchers across Novartis to ‘crowdsource’ a potential weight loss drug. Photo by PJ Kaszas

LIK066 works by blocking two proteins involved in absorbing sugar in the kidneys. One of these proteins is also active in the intestine. The idea is to prevent sugar from being absorbed by the organs, forcing it to be excreted in urine and other bodily waste. Because sugar is an increasingly common source of calories in people’s diets, and the body so effectively converts it into fat, inhibiting these proteins could ultimately lead to weight loss.

But the extent of weight loss in the LIK066 trial was a surprise. “LIK066 seemed to perform better than any other compound that has been tested for the same duration,” Chutkow says.

A crowdsourced solution

That LIK066 came to be tested as a weight loss drug is a story of both innovation and collaboration. After a few years at Novartis, Chutkow took the helm of a team responsible for finding a potential drug to help people lose weight. To improve their odds, he decided to “crowdsource.”

“I set up a summit of sorts, pulling in researchers from across NIBR to see if they knew of any targets we could go after or previous findings that could inform our search,” Chutkow says. “That’s how I learned about LIK066.”

Novartis chemist Greg Bebernitz collaborated with researchers at Advinus Therapeutics to design LIK066 to block two key proteins. Photo by Mingwei Li.

Another team of Novartis translational medicine researchers had evaluated the compound in a separate early-stage clinical trial for type 2 diabetes. During the trial, the researchers had noted a striking side effect: Participants who received the drug experienced unexpected weight loss. After going back and examining the data from that trial, Chutkow's metabolic disease research team concluded that this weight loss was most likely attributable to the compound. In response, NIBR decided to move ahead with a new early-stage clinical trial, this time testing the compound specifically for weight loss in patients with obesity. The researchers are now testing the compound in a larger clinical trial that will run 48 weeks.

In the early-stage trial, patients experienced mild diarrhea from a once-daily dose of the drug. One goal of the 48-week trial is to identify the best dose to maximize weight loss and tolerability, says Andy Bushell, Global Program Head for LIK066 at Novartis Global Drug Development, where he leads the group that is designing and carrying out the larger clinical trials for the compound.

In addition to finding the optimal dose for the compound, Bushell says the next steps in the development process revolve around making sure that any potential medicine derived from LIK066 is designed to meet patient needs. To that end, he initiated a patient advisory forum to solicit input from patient advocates.

"A pill isn't the full solution to the disease of obesity," he notes. "But it would be a key piece of a much-needed, multifaceted approach to improving the health of those living with obesity."

Chutkow eagerly awaits such a product. "As a guy on the front-line treating patients who come into the clinic, I would love to have a new weight loss tool in the toolbox."

Main image: Obesity is a major risk factor for chronic illnesses, but the "eat less, exercise more" approach to weight loss often isn't enough. Image: Pressmaster/Shutterstock.

***Important program update:** Despite early Phase II data showing a positive dose response, the magnitude of the weight loss with LIK066 was not sufficient to deliver transformational benefit to patients as a monotherapy*

in consideration of the evolving marketplace and available treatment options. Novartis has made the decision not to proceed to Phase III with the current program and will therefore begin closing selected clinical studies according to standard regulatory protocols. Novartis is grateful to the LIK066 investigators, trial site personnel, patients and patient advocates whose passion and participation contributed to an outstanding trial design and helped advance our knowledge of weight loss and the metabolic effects of LIK066. Novartis remains committed to developing transformational medicines that help extend and improve the lives of people living with cardio-metabolic diseases.

An experimental #weightloss drug from Novartis has shown early potential.

Research careers at Novartis

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