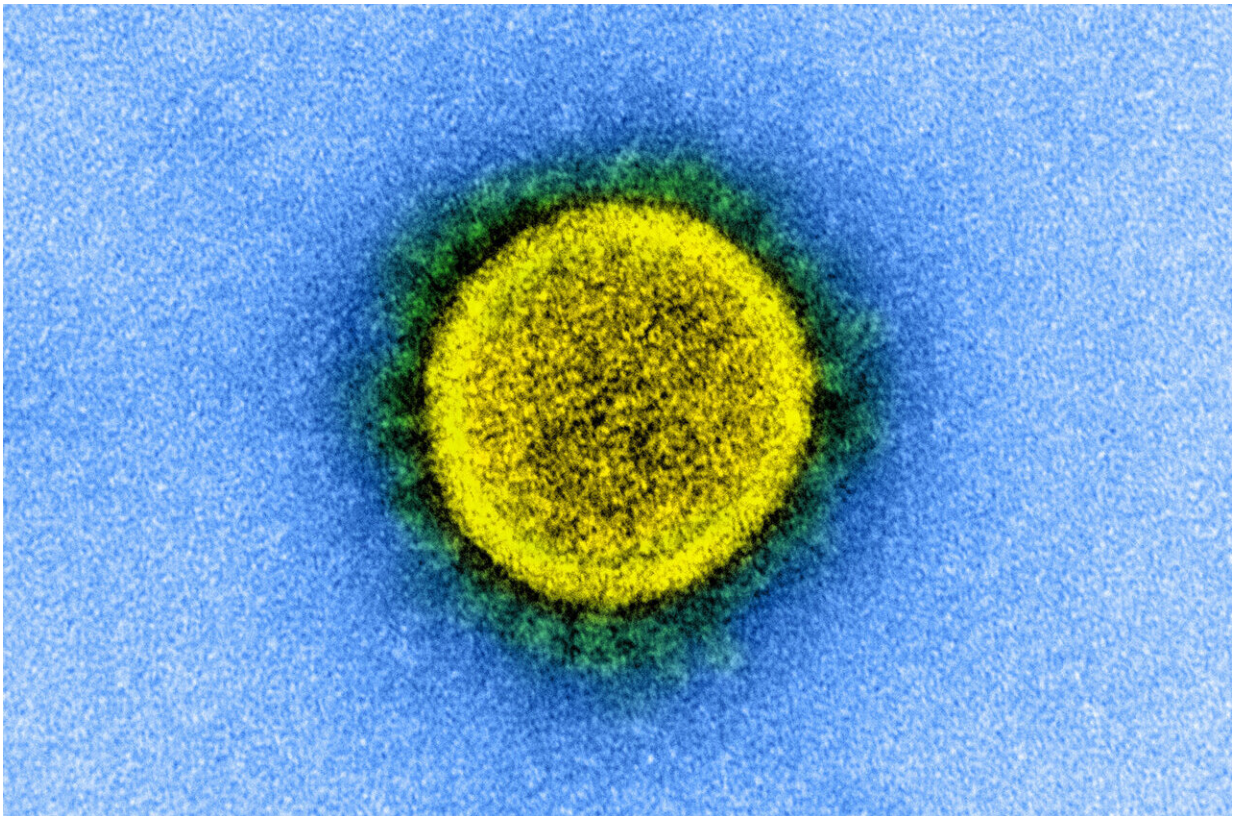


Diabetes drug boosts survival in patients with type 2 diabetes and COVID-19 pneumonia

September 29 2020



SARS-CoV-2 (shown here in an electron microscopy image). Credit: National Institute of Allergy and Infectious Diseases, NIH

Sitagliptin, a drug to lower blood sugar in type 2 diabetes, also improves survival in diabetic patients hospitalized with COVID-19, suggests a

multicenter observational study in Italy. Patients given sitagliptin in addition to insulin had a mortality rate of 18 percent as compared with 37 percent in matched patients receiving only insulin. Led by Paolo Fiorina, MD, Ph.D., of Boston Children's Hospital, the study involved seven Italian hospitals during the first surge of COVID cases last spring.

Although the study was retrospective and observational, the findings—published on September 29 in *Diabetes Care*—have sparked a new randomized, placebo-controlled trial of [sitagliptin](#). That study is now preparing to enroll patients in Europe.

"We think it's reasonable to try sitagliptin if a patient is admitted to the hospital with type 2 [diabetes](#) and COVID," says Fiorina, a diabetes researcher affiliated with the Boston Children's division of nephrology and the University of Milan. "I'm excited about our findings, because we still have very few therapeutic options for the many [diabetic patients](#) affected by COVID."

Based on sitagliptin's mechanism of action, Fiorina and colleagues believe it could also work in nondiabetic patients with COVID. A randomized, controlled trial to test that idea is moving toward regulatory approval.

Why sitagliptin?

Sitagliptin, an oral drug, is one of a class of drugs known as DPP-4 inhibitors, prescribed to an estimated 15 to 20 percent of patients with type 2 diabetes. It was approved by the FDA in 2006, and lowers blood sugar by blocking the receptor for the enzyme DPP-4 (also known as CD26), causing an increase in insulin production.

But recent studies suggest that DPP-4 may also help SARS-CoV-2—the coronavirus that causes COVID-19—get into respiratory cells. In

addition to blocking DPP-4, sitagliptin has anti-inflammatory effects, reducing production of the cytokine IL-6, which is known to contribute to the "cytokine storm" that can cause organ complications in COVID-19.

Sitagliptin may also have a third benefit: keeping [blood sugar](#) down. Previous studies have shown that diabetic patients with worse glycemic control have worse COVID-19 outcomes.

"We decided to try sitagliptin and collect the data," says Fiorina. "COVID-19 mortality in diabetic patients is high, and the drug is very safe, so we felt there was no reason not to use it."

Study design and findings

The study enrolled 338 consecutive patients with type 2 diabetes and COVID-19 pneumonia who were admitted to seven academic hospitals in northern Italy from March 1 through April 30, 2020. Of these, 169 were given only IV insulin for their type 2 diabetes (the standard of care) and served as controls; the other 169 received sitagliptin in addition to IV insulin. The two groups were matched for age and sex, and their outcomes were analyzed retrospectively.

Illness severity, other clinical characteristics, and use of other treatments for COVID-19 were similar in the two groups. Compared with the controls, patients receiving sitagliptin had reduced mortality (18 percent vs. 37 percent) and were more likely to improve clinically.

Specifically, patients treated with sitagliptin were:

- less likely to need [mechanical ventilation](#) (hazard ratio, 0.27, or a 27 percent likelihood as compared with controls)
- less likely to need [intensive care](#) (hazard ratio, 0.51)

- more likely to have at least a 2-point drop on a 7-point scale of disease severity (52 percent, versus 34 percent of controls).
- less likely to have a worsening of clinical outcomes, as defined by any increase in the clinical severity score (26 percent vs. 46 percent).

"We must now confirm our findings in a placebo-controlled, prospective study," says Fiorina. The new trial, enrolling patients in Italy and elsewhere in Europe, can be viewed at [ClinicalTrials.gov: clinicaltrials.gov/ct2/show/NCT04365517](https://clinicaltrials.gov/ct2/show/NCT04365517). The team is also seeking approval to test sitagliptin in COVID-19 patients without diabetes.

Provided by Children's Hospital Boston

Citation: Diabetes drug boosts survival in patients with type 2 diabetes and COVID-19 pneumonia (2020, September 29) retrieved 29 April 2024 from <https://medicalxpress.com/news/2020-09-diabetes-drug-boosts-survival-patients.html>

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