「Plitidepsin Found Almost 30 Times More Potent than Remdesivir in Treating COVID-19」

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In a new study published in Science, a large team of researchers from U.S., France and Spain found in preclinical experiments that Spanish drugmaker PharmaMar's plitidepsin was as much as 27.5 times more effective than remdesivir in treating COVID-19. [1]

As the pandemic has unfolded, medical researchers have looked to drugs already approved by agencies such as the FDA to treat the disease—because using them in new ways is much faster than developing, testing and trialing new drugs. Remdesivir was found in this way to help those afflicted with COVID-19. Unfortunately, remdesivir is not always effective as the many continued deaths from the pandemic have shown. In this new effort, the researchers shifted their focus from drugs like remdesivir, which do their work by attacking proteins on the surface of the SARS-CoV-2 virus, to something new. They looked for drugs that do their work by inhibiting human protein production of proteins that are needed by the virus to survive. [2]

Plitidepsin comes from Aplidium albicans, a sea squirts found only in the waters around the Spanish island of Ibiza and is approved as a cancer drug for multiple myeloma in Australia. In this study, in mice that got plitidepsin shortly before being infected with SARS-CoV-2, the drug significantly reduced viral load and lung inflammation compared with controls. Plitidepsin prompted a reduction in viral load that was on par with remdesivir's, but the cancer drug was better at relieving lung inflammation, the team reported. Plitidepsin shows potent inhibition of SARS-CoV-2, but what's most important is that it works by targeting the host protein rather than the viral protein, meaning the SARS-COV-2 virus will be unable to build resistance through mutation which is a major concern of the new variants. It was originally meant to target the human protein eEF1A, the expression of which can lead to cellular signaling that gives rise to cancer. In the new study, the scientists confirmed that plitidepsin indeed worked against SARS-CoV-2 through inhibition of eEF1A, which interacts with the coronavirus's nucleocapsid (N) protein during an infection. [3]

Surprisingly, in a separate publication paper posted on the journal bioRxiv, the researchers tested plitidepsin against the more highly transmissible B117 variant of SARS-CoV-2. The drug showed similar antiviral activity against both the early-lineage virus and the mutated version in both human gastrointestinal and lung epithelial cell lines, and it was to be about 100 times more potent than remdesivir in human epithelial cells. [4]

These data and the initial positive results from PharmaMar's clinical trial suggests that plitidepsin may

show promise in treating a broad spectrum of antiviral infections, especially those with no clinically approved treatment options, the study authors said. In terms of human clinical trials, PharmaMar already has positive phase 1/2 data for plitidepsin in COVID-19. In October, the company said the clinical trial showed that plitidepsin achieved significant reduction in viral load in hospitalized patients, and a remarkable correlation has been observed between the decrease in viral load and clinical improvement, among other metrics.

Reference:

1. Kris M. White et al. 25 Jan 2021. "Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A" *Science.*
2. Bob Yirka. 29 Jan 2020. "Plitidepsin found to work better than remdesivir for treating COVID-19" *Medical Press.*
3. Angus Liu. 27 Jan 2020. "Cancer drug derived from sea squirts outperforms remdesivir in COVID-19 preclinical models" *Fierce Biotech Press.*
4. Ann-Kathrin Reuschl et al. 24 Jan 2021. "Host-directed therapies against early-lineage SARS-CoV-2 retain efficacy against B.1.1.7 variant" *bioRxiv*