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Remdesivir, a nucleoside analog investigation antiviral drug developed by Gilead Sciences, is being studied in several clinical trials as an experimental treatment for COVID-19. On April 29th, three clinical trials reported their results, which varies slightly depending on different rules of enrolling patients and the endpoint.

The first clinical trial that launched globally was a randomized, double-blind, placebo-controlled, and multi-center study in Hubei, China. It began enrolling patients on Feb 6th, 2020 with 237 patients involved. The result was published in *The Lancet* on April 29th (**China study in patients with severe disease: NCT04257656**). The researchers found that Remdesivir was not associated with statistically significant clinical benefits, but patients receiving the antiviral drug did have a faster time to clinical improvement than those receiving placebo.

The first clinical trial that launched in US was sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) (**NIAID study: NCT04280705**), and they were able to also released the preliminary data analysis and result on April 29th. The data showed that there was a 31% faster time to recovery for the patient who received Remdesivir comparing to the placebo group. It also showed a lower mortality rate of 8.0% versus 11.6% for the group who received placebo.

In addition, Gilead Sciences Inc. released data on a Gilead sponsored Phase 3 simple trial in patients with severe COVID-19 disease on the same day (**Gilead study in patients with severe disease: NCT04292899**). It was a randomized, open-label multi-center study. The data showed that patients who received 5 days of treatment had similar clinical improvements as those who had 10 days of treatment. This data showed the suggested treatment duration for sever patients and helped to make room for other COVID-19 patients who need treatment in ICU.

The reason why those three clinical trials showed varied results is because they had different rules of enrolling patients and different endpoints. The China clinical trial had a more strict requirement for patients, which is that they had to have an interval from symptom onset to enrollment of 12 days or less. Also, the primary endpoint for China trial was the time (in days) from randomization to the point of a decline of two levels on a six-point ordinal scale of clinical status (1=discharged and 6=death). NIAID trial's primary endpoint was time to recovery, which was defined as being well enough for hospital discharge or returning to normal activity level. On May 1st, U.S. Food and Drug Administration (FDA) granted emergency use authorization (EUA) for Remdesivir to treat hospitalized patients with severe COVID-19 virus.

How does Phenomenex fit into all of this?

Phenomenex HPLC preparative columns (ex. AXIA™) and silica gel flash columns (ex. Claricep™) can help to separate and purify compounds during the synthesis of different pro-

drugs and intermediates. Also, the Kinetex® C18, 2.6 µm, 100 ×4.6 mm (Part No. 00D-4462-E0) is recommended to be used in QC for purity assessment during the whole synthesis process of Remdesivir.

Phenomenex was able to run a technical application focusing on the significance of HPLC in the development and production of Remdesivir. You can read more about it in this link or image below: Significance of HPLC in Development and Products of the Antiviral Drug Remdesivir

APPLICATIONS

Significance of HPLC in the Development and Production of the Antiviral Drug Remdesivir

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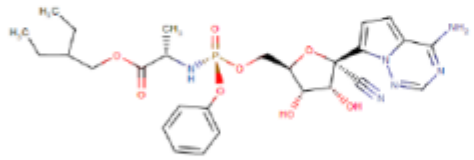
Overview

The disease COVID-19 caused by the new coronavirus SARS-Cov-2 is now classified as a pandemic outbreak by the World Health Organization (WHO). After Chinese researchers identified the pathogen and shared viral genomic sequences in a short period of time, many drug-research institutes began screening different classes of antiviral drugs. However, no specific single therapeutic has appeared to fully treat the virus infection so far. On January 31, 2020, the New England Journal of Medicine (NEJM) published an article about the first case of a COVID-19 infected person being cured in the United States[1], which raises hope for the development of new anti-coronavirus specific drugs.

Remdesivir, the drug mentioned in the article, is also known as GS-5734. It is a nucleoside analog antiviral drug developed by Gilead Sciences. According to an article published in the Journal of Medicinal Chemistry[2], within more than 20 years of research spanning multiple antiviral drug projects, GS-5734 stands out from the drug library of nearly 1,000 different nucleosides and nucleoside phosphates as it demonstrates high potency in multiple cell lines and has the potential to scale up due to its rapid synthesis process.

Figure 1. Structure of Remdesivir (*Drug Bank*)



Nucleoside analogs are activated by intracellular nucleoside kinases to produce their respective nucleoside triphosphate (NTP). The pharmacologically active NTP then competes with the endogenous natural nucleotide library to be incorporated into replicated viral RNA and acts as a RNA chain terminator. As the first phosphorylation step to generate nucleoside monophosphate is usually a rate-limiting step, monophosphate prodrugs, especially phosphoramidates, have been widely studied in the screening of nucleoside analogs. Structure-wise, Remdesivir is obtained by the monophosphorylation of nucleoside analogs, and the 1'-CN group and C-linked nucleobases are important for selective resistance to host polymerase.

This article[2] proposes a more efficient route for the synthesis of the single Sp diastereomer- GS-5734 by the crystallization of a key reagent. The synthesized GS-5734 molecule was then subjected to in-vivo model study. HPLC was used for purity assessment during the whole synthesis process. The column used in this article was Kinetex® C18, 2.6 µm, 100 × 4.6 mm (Part No. 00D-4462-E0). A gradient from 2% mobile phase B to 98% mobile phase B was performed under the conditions of 0.1% TFA in water as mobile phase A, 0.1% TFA in acetonitrile as mobile phase B, and a flow rate of 1.5 mL/min. The core-shell structure of Kinetex column results in narrower peak shapes and shorter run time for purity assessment.

Have any questions regarding the above or Remdesivir? Chat with our technical specialists, like Grace, nearly 24/7 around the world through our online technical support service, Chat Now. Our specialists will be able to help you with any technical questions, method optimization tips, and even receive a quote for product recommendations.

Click the link to start chatting now: Chat Now

**Phenomenex does not have any affiliation with the clinical studies or companies mentioned in the article above*

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