

# The STORM-C-1 trial

## Interim results of the STORM-C-1 trial of ravidasvir plus sofosbuvir in patients with chronic hepatitis C infection

This is a summary of the following peer-reviewed scientific article:

### **Efficacy and safety of ravidasvir plus sofosbuvir in patients with chronic hepatitis C infection without cirrhosis or with compensated cirrhosis (STORM-C-1): interim analysis of a two-stage, open-label, multicentre, single arm, phase 2/3 trial**

Andrieux-Meyer I, Tan S-S, Thanprasertsuk S, Salvadori N, Men  trety C, Simon F, Cressey TR, Said HRHM, Hassan MRA, Omar H, Tee H-P, Chan WK, Kumar S, Thongsawat S, Thetket K, Avihingsanon A, Khemnark S, Yerly S, Ngo-Giang-Huong N, Siva S, Swanson A, Goyal V, Bompert F, P  coul B, Murad S *The Lancet Gastroenterology and Hepatology* 2021  
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## 1 WHY WAS THIS STUDY DONE?

The STORM-C-1 study was designed to evaluate the efficacy and safety of the new drug ravidasvir, developed by a public-private partnership, for use with sofosbuvir, an existing drug, with the goal of providing an affordable option for the safe and effective treatment of hepatitis C virus (HCV) infection.

Both drugs are direct-acting antivirals (DAAs), part of a new generation of powerful hepatitis C treatments that can cure patients in three to six months. The previous standard therapy required a year of treatment that often had severe side effects and only a 50% treatment success rate. The new drug combinations represent an important advance in the treatment of HCV infection. However, DAAs are prohibitively expensive in countries that are not licensed to produce or sell cheaper generic versions or that do not have special reduced pricing arrangements for originator drugs.

HCV, which can lead to chronic liver disease, cirrhosis, cancer, and death, affects about 58 million people worldwide, but only an estimated 13% have received treatment with DAAs to date. The disease causes around 300,000 deaths a year.

There is a need for an affordable, effective, and safe HCV treatment regimen for all genotypes to complement other regimens, appropriate for patients who are also taking antiretroviral treatment for HIV, and that is simple and suitable for use in decentralised healthcare settings.

Ravidasvir was developed by the US biopharmaceutical company Presidio Pharmaceuticals and identified by DNDi as having the potential to be developed for the treatment of HCV at an affordable price. In 2016, Presidio Pharmaceuticals, DNDi, and the Egyptian generics manufacturer Pharco Pharmaceuticals signed a licence agreement to secure supplies of ravidasvir and sofosbuvir for the study.

Before the STORM-C-1 study, there was little evidence on the efficacy of ravidasvir in patients with HCV. There were some studies in people with genotypes 1 and 4, but data on the efficacy and safety of ravidasvir plus sofosbuvir in patients with other HCV genotypes were not available. Globally, the two most prevalent genotypes of HCV are genotype 1 (44% of infections),

which is more prevalent in high-income countries, and genotype 3 (25% of infections), which is more prevalent in low- and middle-income countries and is harder to treat with DAAs.

## 2 WHAT WAS EVALUATED AND HOW?

The STORM-C-1 study was designed in two stages to allow for interim analysis and presentation of results after the first stage. This is a summary of the publication describing the results of the first stage. In this study, we investigated the safety and efficacy of a ravidasvir plus sofosbuvir regimen in a diverse group of patients with HCV, with or without cirrhosis.



We recruited 301 adult patients with HCV in six centres in Malaysia and four centres in Thailand. The patient group was diverse and included people living with and without HIV, who had had previous interferon-based HCV treatment or not, and with any genotype. Patients with liver cirrhosis were given the treatment (200 mg ravidasvir and 400 mg sofosbuvir once a day) for 24 weeks, while those without cirrhosis received it for 12 weeks. Then, 12 weeks after the end of treatment we tested whether there was any HCV virus left in the body by testing for virus RNA. We also took blood samples from patients also living with HIV to determine whether the RDV-SOF treatment had any effect on the levels of HIV medication they were already taking.

**3 WHAT WERE THE RESULTS?**

About half of the patients we enrolled had genotype 3 HCV infection (which is harder to treat), and the others had genotypes 1a, 1b, 2 and 6. Just over a quarter had compensated cirrhosis of the liver, nearly a third were also infected with HIV, and a third had previously been treated with interferon. All enrolled patients received at least one dose of the study drug; no patients were lost to follow-up, but six discontinued treatment.

**Efficacy:** Treatment in 301 patients without and with compensated cirrhosis was efficacious, regardless of HIV infection and previous interferon experience: 97% of patients had no detectable HCV RNA detectable 12 weeks after the end of treatment. The low rate of unsuccessful treatments (in particular for difficult-to-treat genotype 3 infection) is significant, in particular for countries where access to salvage therapies is restricted and expensive.

**Safety:** The treatment was well-tolerated and overall adherence rates were consistently high throughout the study and in all groups, making it an appropriate treatment for broad use.

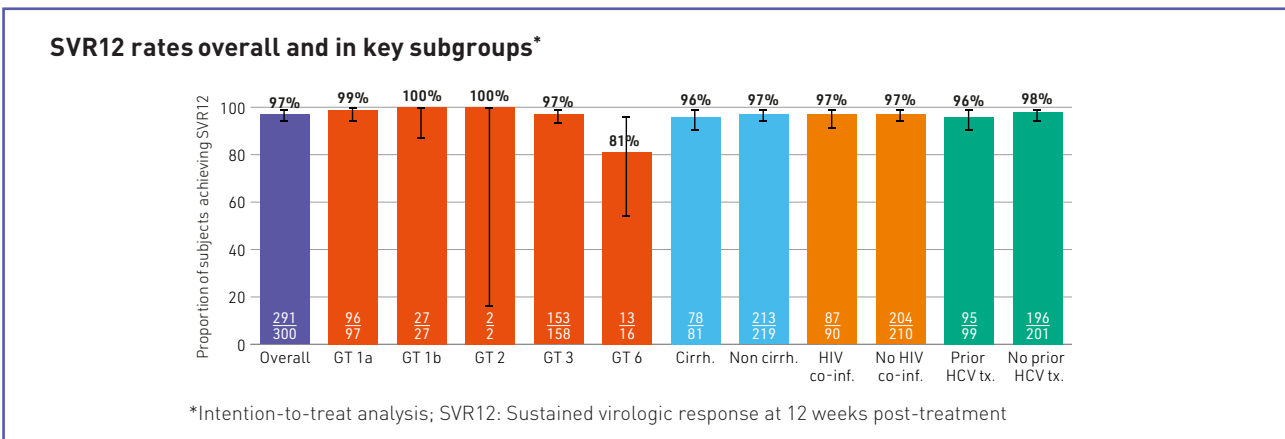
**HIV coinfection:** The HCV drug daclatasvir interacts with HIV antiretroviral treatments, which means that either the HIV treatment or the daclatasvir dose has to be changed when treating HIV-coinfected patients for HCV. In our study, no clinically significant drug-drug interactions between ravidasvir plus sofosbuvir and antiretrovirals commonly

used in the region were found, and no antiretroviral dose adjustments were needed, making this treatment suitable for patients also living with HIV.

**4 WHAT DOES THIS MEAN FOR PEOPLE WITH HCV?**

The results show that the ravidasvir plus sofosbuvir combination could provide an affordable, simple, and effective public health tool to contribute to the elimination of HCV as a cause of illness and death in countries that do not have, or have overcome, sofosbuvir patent barriers. Because the ravidasvir plus sofosbuvir combination appears to be suitable for use in diverse populations, including people living with HIV, it could minimize the need for pre-treatment assessments and on-treatment monitoring, allowing the management of HCV in decentralized health settings under the supervision of appropriately trained healthcare professionals already taking.

A commentary\* on this study points out that although reducing the cost of DAA treatment is important, other barriers to achieving the WHO 2030 HCV elimination targets remain, including the limited availability and affordability of diagnostics, the lack of high-quality surveillance data, and the need to restructure many health systems. Crucially, a strong political commitment is needed to support public health programmes and to make HCV treatment available and affordable, as has been seen in Malaysia.



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**CLINICAL TRIAL REGISTRATION:** This trial is registered with ClinicalTrials.gov, number NCT02961426, and the National Medical Research Register of Malaysia, NMRR-16-747-29183.

\* **Affordable treatment and political commitment are crucial to eliminate hepatitis C globally** Hellard M, Pedrana A, Draper B *The Lancet Gastroenterology and Hepatology* 2021 [https://doi.org/10.1016/S2468-1253\(21\)00135-7](https://doi.org/10.1016/S2468-1253(21)00135-7)