COSMOS Study Results:[i]

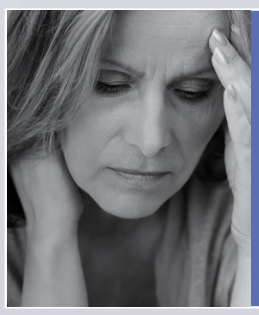
Efficacy and Safety of Simeprevir in Combination with Sofosbuvir, Once-Daily, for Genotype 1 Chronic Hepatitis C

Global Burden of Hepatitis C

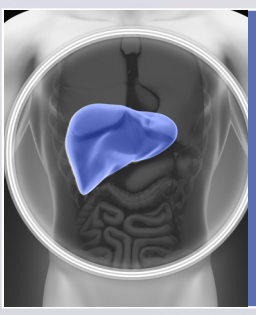
150 MILLION people are infected with hepatitis C virus (HCV) worldwide, which is **OVER 2%** of the world's population[ii]

Up to 500,000 people die from the disease every year[ii]

In Europe there are an estimated 9 MILLION PEOPLE infected by HCV and approximately **86,000 HCV-related deaths** occur EACH YEAR[iv]



The current evidence suggests that HCV has been associated with **tremendous clinical, economic and quality of life burden**[vi]



HCV remains the **LEADING CAUSE of liver cancer, liver disease and liver transplantation,** placing a huge burden on patients' lives and healthcare systems.[vii]

MORE INFORMATION ON HCV CAN BE FOUND BY VISITING:
The World Health Organization, *www.who.int*
World Hepatitis Alliance, *www.worldhepatitisalliance.org/en*
European Liver Patients Association, *www.elpa-info.org*

PROGRESSION OF UNTREATED HEPATITIS C OVER TIME[iii]

For Every 100 people infected with HCV

75–85 will develop **chronic infection**

60–70 will develop **liver disease**

5–20 will develop **cirrhosis**

1–5 will likely **die of cirrhosis or liver cancer**

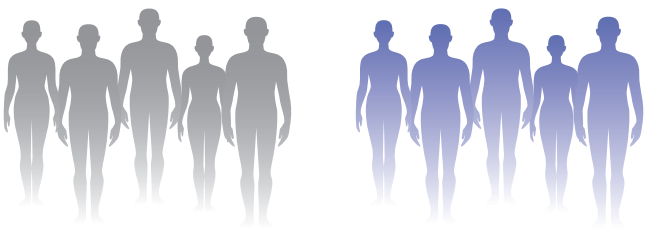
COSMOS Study[i]

(**C**ombination **O**f **S**i**M**eprevir and s**O**fosbuvir in HCV genotype 1 infected patient**S**)

OVERVIEW

The Phase 2 COSMOS study investigated simeprevir, a once-daily, HCV NS3/4A protease inhibitor, in combination with sofosbuvir, a nucleotide analogue NS5B polymerase inhibitor, developed by Gilead Sciences, Inc., without or with ribavirin for chronic HCV genotype 1 infection, including patients with compensated cirrhosis.

METHODOLOGY



Cohort 1

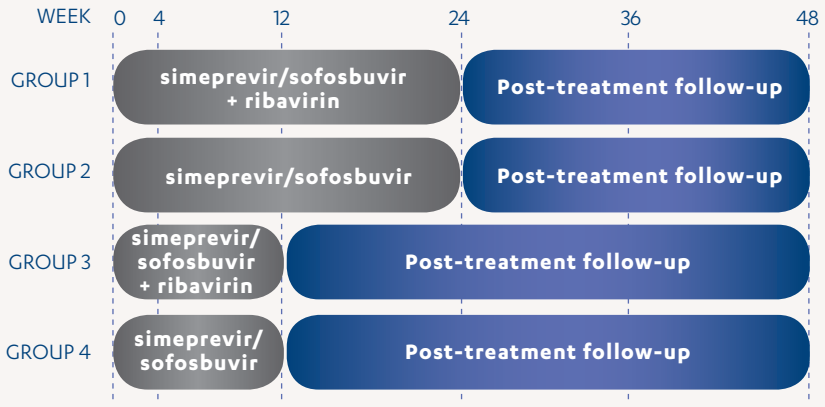
Prior null-responder patients who did not respond to treatment with peginterferon and ribavirin with no to moderate liver fibrosis (defined as METAVIR F0 to F2 scores).

Cohort 2

Treatment-naïve and prior null-responder patients with advanced fibrosis, including cirrhosis (defined as METAVIR F3 to F4 scores).

The METAVIR score is a measure to quantify the degree of fibrosis and inflammation of liver disease.

Patients were randomly assigned to one of four treatment groups and treated for 12 or 24 weeks



simeprevir 150 mg once-daily + sofosbuvir 400 mg once-daily ± ribavirin 1000/1200 mg/day twice-daily

The primary endpoint was sustained virologic response 12 weeks after completing treatment (SVR12), defined as HCV RNA not detectable in the blood.

SVR is an important indicator that correlates strongly with a clearance of HCV, and effectively a cure.[viii]

RESULTS

The all-oral, interferon-free treatment regimen with simeprevir and sofosbuvir resulted in an overall SVR12 rate of 92%, consistent SVR12 rates regardless of METAVIR score, and was an effective and well-tolerated therapeutic regimen in both treatment-naïve and prior null-responder patients.

SVR12 among patients treated for 12 weeks

Cohort 1	Cohort 2
93% treated with simeprevir/sofosbuvir	**93%** treated with simeprevir/sofosbuvir
96% treated with simeprevir/sofosbuvir + ribavirin	**93%** treated with simeprevir/sofosbuvir + ribavirin

Among patients with compensated cirrhosis (METAVIR F4 score), **86 percent** of patients treated with simeprevir/ sofosbuvir and **91 percent** of patients treated with simeprevir/ sofosbuvir + ribavirin **achieved SVR12.**[ix]

* Extending treatment duration from 12 to 24 weeks and the addition of ribavirin did not clearly improve SVR12 rates

In the COSMOS trial, the most common (> 10 percent) adverse events reported during treatment with simeprevir in combination with sofosbuvir without and with ribavirin were fatigue (31 percent), headache (20 percent), and nausea (16 percent).

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iv. Hatzakis A et. al. The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference. Journal of Viral Hepatitis, 2011:18,1-16.
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ix. Lawitz E et al. Simeprevir plus sofosbuvir with/without ribavirin for treating chronic 1 HCV genotype 1 infection in prior null-responders to 2 peginterferon/ribavirin and treatment-naïve patients (COSMOS: a 3 randomised study). Appendix P1. Lancet 2014, doi.org/10.1016/S0140-6736(14)61036-9

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