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New data for HCV genotype 4 patients with simeprevir- and sofosbuvir-based regimens

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Results from RESTORE , a phase III, multicentre, single-arm, open-label study presented today at the International Liver Congress 2014 showed that simeprevir 150 mg once-daily for 12 weeks in combination with peginterferon and ribavirin (followed by 12 or 36 weeks of peginterferon and ribavirin) was effective and well tolerated in hepatitis C virus (HCV) genotype 4-infected patients, consistent with previous observations in HCV genotype 1-infected patients.

Overall, 65.4% of patients achieved SVR12 (82.9% of treatment-naïve, 86.4% of prior-relapser, 60.0% of prior partial-responder and 40.0% of prior null-responder patients). The rapid virological response (RVR) rates in the IL28B CT and TT patient sub-groups were 65.5% and 62.2%, respectively, while 65.6% and 59.5% achieved SVR12, respectively. Among those patients with more severe liver fibrosis (METAVIR score F4), 62.1% and 46.7% achieved RVR and SVR12, respectively.

Response-guided therapy criteria used to identify patients eligible for a total treatment duration of 24 weeks were met by 88.6% and 90.9% of treatment-naïve and prior-relapser patients, respectively. Among them, 93.5% and 95.0%, respectively, achieved SVR12. No patients meeting response-guided therapy criteria experienced on-treatment failure, while three patients experienced viral relapse (treatment-naive, n=2; relapsers, n=1).

"HCV genotype 4 is a strain of virus which currently only has limited

treatment options," said EASL's Secretary General Professor Markus Peck-Radosavljevic. "We therefore welcome these positive results for the simeprevir-based regimen."

Although HCV genotype 4 is mainly found in the Middle East, Egypt and Central Africa, it has recently spread in several Western countries, particularly in Europe, with rates of 10% to 24%.

Overall simeprevir was well tolerated; most adverse events (AEs) were grade 1 or 2. Serious AEs were infrequent (five patients [4.7%]; no deaths) and considered unrelated to simeprevir. Most frequent AEs (>30% of patients) included influenza-like illness, asthenia and fatigue.

In this phase III study conducted in France and Belgium, 107 patients with chronic HCV genotype 4 received simeprevir once daily with peginterferon and ribavirin for 12 weeks. Treatment-naïve and prior-relapser patients received response-guided therapy with peginterferon and ribavirin continued for up to 24 or 48 weeks. Prior partial responders and prior null responders continued to receive peginterferon and ribavirin for 48 weeks.

Out of a total patient population of 107 patients, 35 were treatment-naïve, 22 relapsers, 10 partial responders, and 40 null responders. The demographics of the patient population were as follows: 78.5% male; median age, 49 years; 28.0% Black; 28.8% METAVIR F4; 92.5% IL28B non-CC host genotype; and 42.5/23.6/33.9% HCV GT4a/4d/4other genotype.

Simeprevir is an NS3/4A protease inhibitor jointly developed by Janssen R&D Ireland and Medivir AB, with antiviral activity against HCV genotypes 1, 2, 4, 5 and 6, and approved in Japan, Canada, the United States and Russia for the treatment of chronic hepatitis C infection in combination with pegylated interferon and ribavirin in HCV genotype

1-infected patients with compensated liver disease, including cirrhosis. Taken as one capsule, once-daily, simeprevir works by blocking the protease enzyme that enables HCV to replicate in host cells.

Patients of Egyptian ancestry infected with Genotype 4 HCV achieve high virological response rates with sofosbuvir plus ribavirin

In a second study involving treatment-naive and treatment-experienced patients of Egyptian ancestry with chronic genotype 4 HCV infection, sofosbuvir plus ribavirin was shown to provide a simple, effective, and well-tolerated, interferon-free regimen.

After 12 weeks of treatment with sofosbuvir plus ribavirin, SVR12 rates were 79% (11/14) in treatment-naïve patients and 59% (10/17) in treatment-experienced patients. Extending treatment duration to 24 weeks resulted in higher SVR12 rates in both treatment-naïve and -experienced patients: 100% (14/14) and 87% (13/15) respectively.

Relapse accounted for all virological failures except in one treatment-naïve subject receiving 12 weeks treatment who had a partial response.

Most AEs were mild or moderate in severity and consistent with the known side effects of ribavirin.

Presenting these results, Professor Peck-Radosavljevic said "the current treatment for GT4 is sofosbuvir + pegylated interferon + ribavirin for 12 weeks which resulted in a 96% (27/28) SVR12 rate in the Phase 3 NEUTRINO trial.

"What makes the results from this new study with sofosbuvir so important is that it included those patients who were interferon-ineligible, -intolerant, and failures, where a significant unmet medical need exists", Professor Peck-Radosavljevic added.

In this study, patients, born in Egypt and of Egyptian ancestry, with chronic HCV GT4 infection were randomised 1:1, stratified by prior treatment status and cirrhosis status, to receive 12 or 24 weeks sofosbuvir (400 mg/day) + ribavirin (1000-1200 mg/day). Approximately 20% could have compensated cirrhosis.

Of the 60 patients enrolled, 28 were treatment-naïve and 32 treatment-experienced. 68% were male, 23% cirrhotic, and 17% had the IL28B CC host genotype.

Sofosbuvir is a nucleotide polymerase inhibitor with a high barrier to resistance that is taken as an oral, once-daily formulation. With activity against HCV genotypes 1-6, in-vitro activity of sofosbuvir against genotype 4a HCV has been shown to be similar to its activity against other HCV genotypes. With more than 3000 patients treated to date, sofosbuvir appears to be safe and well tolerated.

More information: 1. MORENO ET AL. ONCE-DAILY SIMEPREVIR (TMC435) WITH PEGINTERFERON/RIBAVIRIN IN TREATMENT-NAÏVE OR TREATMENT-EXPERIENCED CHRONIC HCV GENOTYPE 4-INFECTED PATIENTS: SVR12 RESULTS OF A PHASE III TRIAL. ABSTRACT PRESENTED AT THE INTERNATIONAL LIVER CONGRESS 2014

2. ESTEBAN JI, SAULEDA S, QUER J. THE CHANGING EPIDEMIOLOGY OF HEPATITIS C VIRUS INFECTION IN EUROPE. J HEPATOL. 2008; 48 (1): 148-162.

3. RUANE, P.J ET AL. SOFOSBUVIR PLUS RIBAVIRIN, AN INTERFERON-FREE REGIMEN, IN THE TREATMENT OF TREATMENT-NAÏVE AND TREATMENT-EXPERIENCED PATIENTS WITH CHRONIC GENOTYPE 4 HCV INFECTION ABSTRACT PRESENTED AT THE INTERNATIONAL LIVER

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