Optimization of an Interferon-free Hepatitis C Virus Therapy Regimen Containing the HCV NS3/4A Protease Inhibitor Faldaprevir, the Non-nucleoside NS5B Inhibitor Deleobuvir, and Ribavirin for Genotype-1b-infected Patients

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INTRODUCTION

• New direct acting antivirals (DAAs) currently in development for treatment of chronic hepatitis C virus (HCV) are being tested in conjunction with and without both pegylated interferon-alpha and ribavirin (PegIFN/RBV)

RATIONALS

• The aim of SOUND-C3 was to optimize IFN-free treatment with faldaprevir, deleobuvir, and RBV following the SOUND-C2 study

• SOUND-C2, investigating the safety, efficacy, and treatment duration of faldaprevir 120 mg QD, deleobuvir 600 mg BID with or without RBV for 16, 28, or 40 weeks in 382 genotype 1b-infected patients

• Cirrhotic patients were included and accounted for 9% of the total population

• Patients infected with HCV GT-1a who received faldaprevir 120 mg QD, deleobuvir 600 mg BID, and RBV achieved an SVR12 rate of 85%

• Patients with compensated liver cirrhosis were eligible and accounted for 31% of the population

• The interferon-free combination of faldaprevir, deleobuvir, and RBV for 16 weeks was highly efficacious in patients infected with HCV GT-1b with SVR12 rates of 96% (Figure 5)

• Eight GT-1a treatment-naïve patients experienced rebound or relapse, two patients were below the limit of detection (BLD) (≤10 IU/mL) at SVR12 follow-up, and one patient did not complete follow-up (Figure 4)

• Adverse events and worst-on-treatment changes in laboratory values are shown in Tables 2 and 3

• The interferon-free combination of faldaprevir, deleobuvir, and RBV for 16 weeks was highly efficacious in patients infected with HCV GT-1b with SVR12 rates of 96%

• All four GT-1b-infected patients with cirrhosis achieved SVR12

• The combination of faldaprevir, deleobuvir, and RBV was well tolerated with few discontinuations due to AEs

• Viral response in GT-1a-infected patients was significantly lower

RESULTS

• The interferon-free combination of faldaprevir, deleobuvir, and RBV for 16 weeks was highly efficacious in patients infected with HCV GT-1b with SVR12 rates of 96% (Figure 5)

• One GT-1b-infected patient discontinued treatment at Day 69 due to AEs, did not achieve SVR12, and subsequently relapsed

• Another GT-1b-infected patient discontinued treatment early at Day 41 due to AEs but went on to achieve SVR12

• Eight GT-1a treatment-naïve patients experienced rebound or relapse, two patients were below the limit of detection (BLD) (≤10 IU/mL) at SVR12 follow-up, and one patient did not complete follow-up (Figure 4)

• Adverse events and worst-on-treatment changes in laboratory values are shown in Tables 2 and 3

METHODS

• The Phase 3b SND-C3 study (N=32) tested the BID regimen from SOUND-C2 for a period of only 16 weeks (Figure 4). The primary endpoint was SVR12, and patients with compensated liver cirrhosis were eligible and accounted for 31% of the population

• Treatment-naïve GT-1a patients (n=12) carrying the UGT1A1*28 genotype were treated with faldaprevir 120 mg QD + deleobuvir 600 mg BID

• No loading dose of deleobuvir was administered on Day 1 in SOUND-C3

• Baseline characteristics are shown in Table 1

• The interferon-free combination of faldaprevir, deleobuvir, and RBV for 16 weeks was highly efficacious in patients infected with HCV GT-1b with SVR12 rates of 96%

• Eight GT-1a-infected patients with cirrhosis achieved SVR12

• The combination of faldaprevir, deleobuvir, and RBV was well tolerated with few discontinuations due to AEs

• Viral response in GT-1a-infected patients was significantly lower