Poster No.83

THE EFFICACY AND SAFETY OF RAVIDASVIR PLUS SOFOSBUVIR IN ADULTS WITH CHRONIC HEPATITIS C WITHOUT CIRRHOSIS OR WITH COMPENSATED CIRRHOSIS : FINAL RESULTS OF STORM-C 1, A PHASE 2/3 TRIAL IN MALAYSIA AND THAILAND

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Introduction : Simple direct-acting anti-viral regimens are one of the key tools for national scale-up of hepatitis C (HCV) treatment to achieve its elimination. Ravidasvir is a highly potent NS5A inhibitor with pan-genotypic potential. We aim to assess the safety and efficacy of ravidasvir plus sofosbuvir in adults with HCV infection in Malaysia and Thailand.

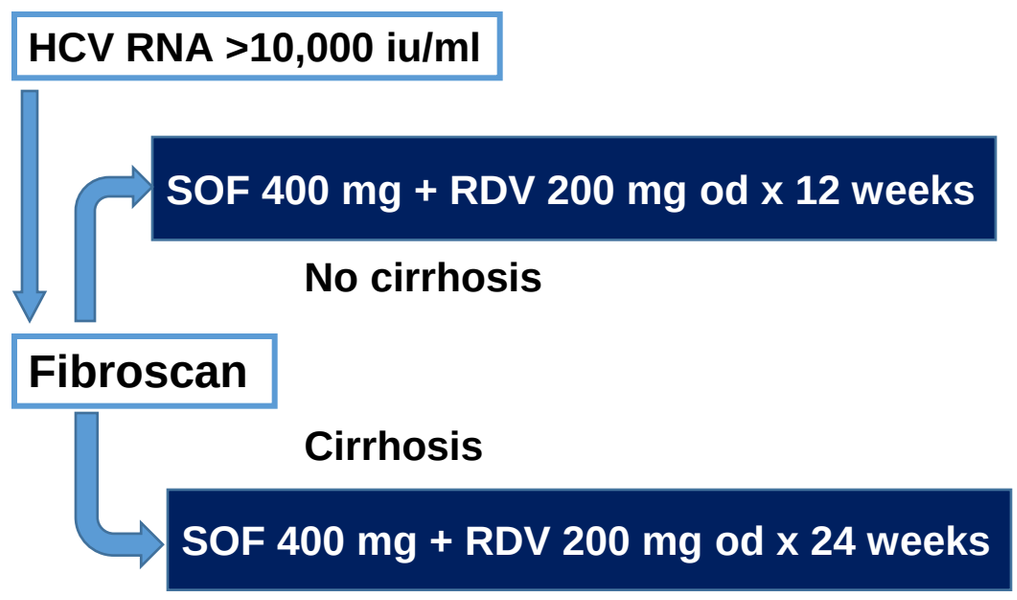
Materials and methods: Open-label, phase 2/3 single-arm clinical trial conducted in 13 public hospitals in Malaysia and Thailand. Once daily ravidasvir (200 mg) and sofosbuvir (400 mg) for 12 weeks were given for patients without cirrhosis and 24 weeks for those with compensated cirrhosis, Child Pugh Score A. The diagnosis of cirrhosis was by liver stiffness measurement by transient elastography >12·5 kPa (M probe) or >10 kPa (XL probe) or liver biopsy or APRI ≥ 2 in their absence.

Inclusion criteria: Chronic hepatitis C with HCVRNA ≥10^4 IU/ml, of any genotype, aged 18–69 years, BMI 18–35 kg/m^2, without cirrhosis or with compensated cirrhosis, without or with virologically controlled HIV co-infection, treatment naïve or interferon ± ribavirin experienced. Women of childbearing potential with a negative pregnancy test and non-injecting drug users, including participants compliant in opioid substitution maintenance programme.

Exclusion criteria: Patients with decompensated cirrhosis or hepatocellular carcinoma or hepatitis B virus co-infection or serum creatinine >1·5 XULN or end stage renal disease, or prior NS5A inhibitor therapy.

On-treatment visits: at weeks 1, 4, 8, and 12
(additional visits at weeks 16, 20, and 24 for cirrhosis).
Post-treatment visits: at weeks 4, 12, and 24 after treatment completion.

Routine bloods, urine, ECG, assessment for adverse events and Child Pugh score. Sustained virological response at 12 weeks post treatment (SVR12) was defined as HCVRNA < 12 iu/ml or <15 iu/ml.

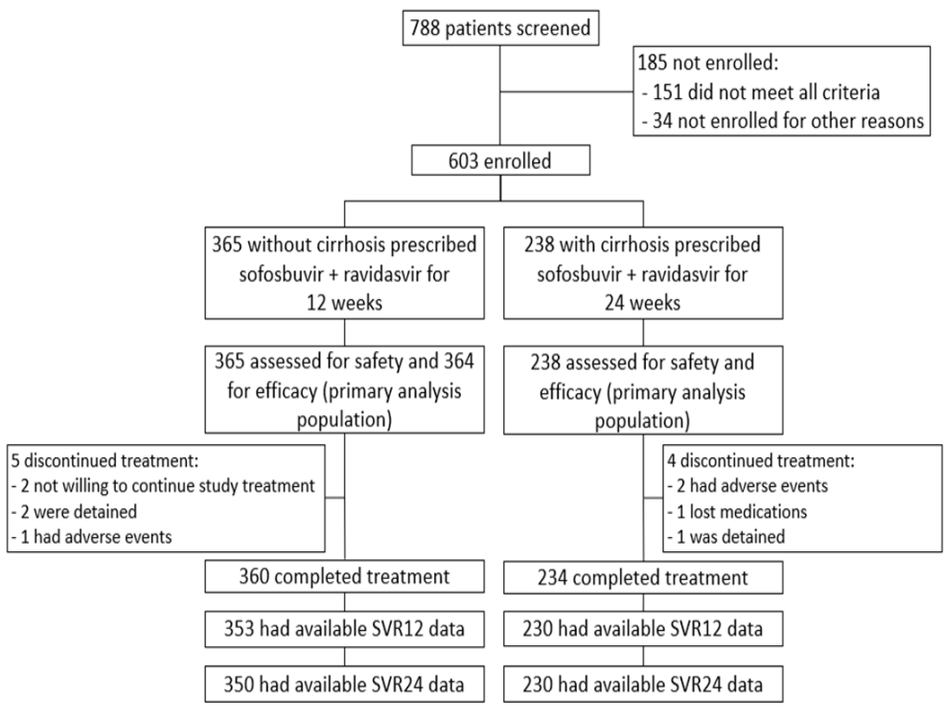


Results: Between September 2016 and September 2020, 603 participants (Malaysia=397, Thailand=206) were enrolled in 2 stages.

Table 1 : Baseline characteristics

Parameters	Results (%)
Male	472 (78%)
Median age in years (range)	47 (20-67)
Cirrhosis	238 (39%)
HIV co-infection	192 (32%)
Prior interferon±ribavirin	120 (20%)

Figure 1 : Study patients flow



Reasons for non-enrollment: clinically significant findings or unstable condition, Covid-19 epidemic, HCVRNA <10,000 IU/mL, HIVRNA > 50 copies/mL, direct bilirubin > 3xULN, CTP B or C, QTcF ≥ 450 ms

Table 2 : Adverse events

Parameter	Overall (N=603)
Treatment-emergent AE (TEAE)	333 (55%)
TEAE of Grade 1	263 (44%)
TEAE of Grade 2	160 (27%)
TEAE of Grade 3 or higher	35 (6%)
Treatment-related TEAE of Grade 3 or higher	5 (1%)
TEAE of Grade 4	2 (<1%)
Treatment-related TEAE of Grade 4	0 (0%)
Treatment-related TEAE resulting in death	0 (0%)
Treatment-related TEAE leading to permanent treatment discontinuation	2 (<1%)
Treatment –emergent serious AE (TESAE)	35 (6%)
Treatment related TESAE	1(<1%)

Adverse events occurring in ≥ 5% : pyrexia (8%), URTI (6%), cough (6%), dizziness (5%), headache (5%).

Figure 2 : Sustained Virological Response at week 12 post treatment by ITT analysis

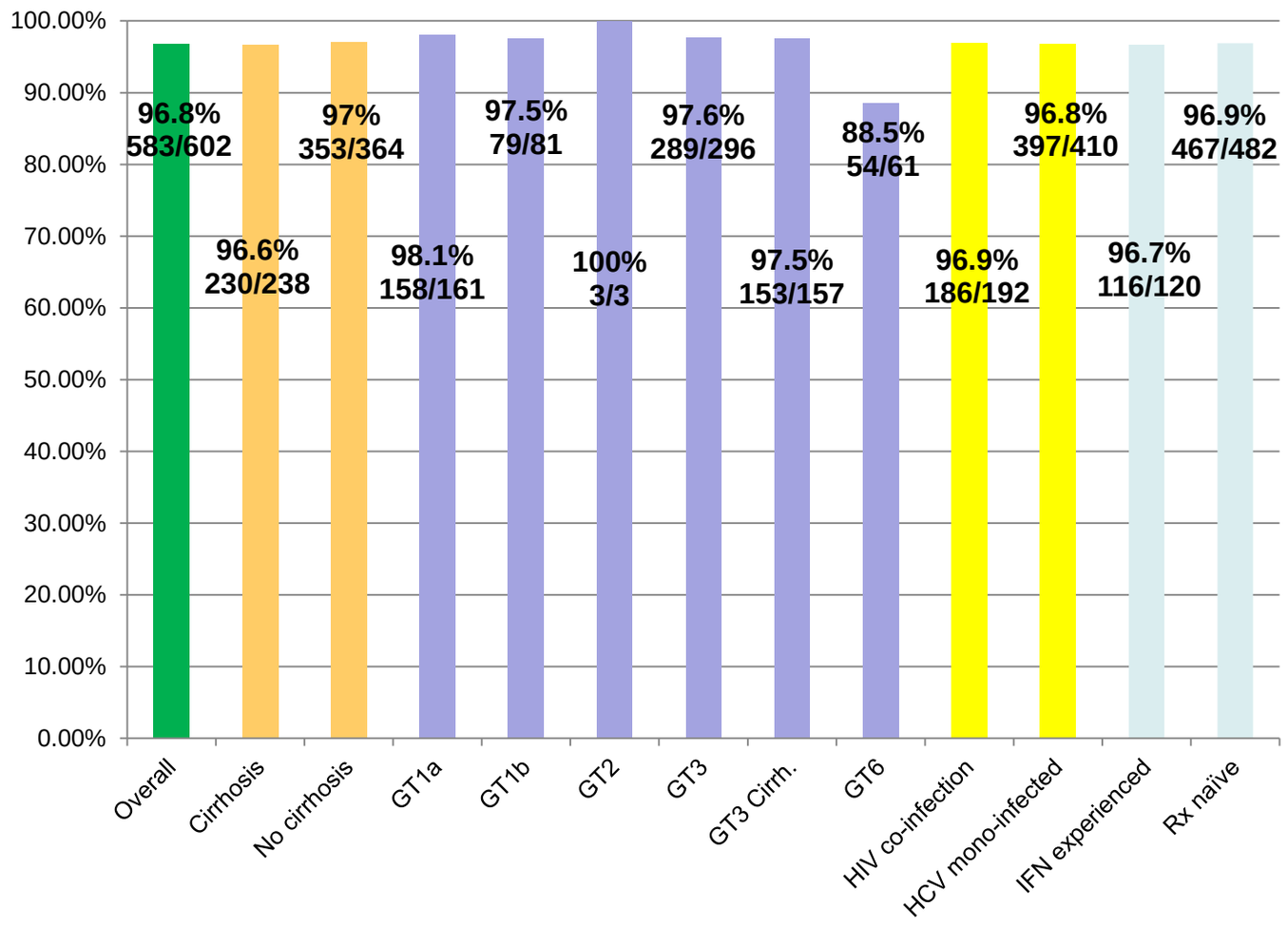


Table 3: Reasons for failed SVR12, n= 19 (3.2%)

Non virological failure	7 (1.2%)
Virological failure • Virological breakthrough, • Virological relapse	12 (2.0%) • 3 (0.5%) • 9 (1.5%)

Discussion / Conclusion

Ravidasvir plus sofosbuvir for 12 or 24 weeks has excellent safety and efficacy in adult HCV infections with no cirrhosis or compensated cirrhosis.

This ribavirin-free DAA regimen also provided high SVR12 in the difficult to treat HCV genotype 3 with cirrhosis.

With treatment regimen determined by the presence of cirrhosis and the high tolerability, simplifications of HCV management and treatment programs are feasible.

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