Ravidasvir in combination with sofosbuvir for 12 or 24 weeks achieved high sustained virological response rates in genotype 3 chronic hepatitis C without or with compensated liver cirrhosis

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Introduction

Hepatitis C virus (HCV) genotype 3:

- The second most common HCV genotype with approximately 14-17 million cases globally.
- Associated with injecting drug use (IDU), the primary mode of HCV transmission, with more severe liver disease and a lower sustained virological response (SVR), especially in patients with cirrhosis, even in the era of direct-acting antiviral therapies.

Ravidasvir:

- Potent NS5A inhibitor with no clinically significant interaction with CYP P450.
- Recently added to the WHO Model Lists of Essential Medicines for treatment of HCV in combination with sofosbuvir.

Aim

To analyze the genotype 3 cohort of the phase 2/3 STORM-C-1 trial to determine the efficacy in this subpopulation.

Method

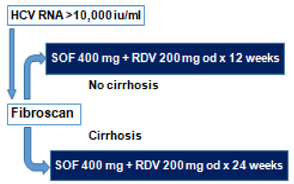
Open-label, single-arm Phase 2/3 study in people with chronic HCV +/- HIV infections of all genotypes in Malaysia and Thailand.

Inclusion criteria: Chronic HCV with HCVRNA ≥10^4 IU/ml, any genotype, aged 18–69 years, without cirrhosis/ with compensated cirrhosis, without/ with virologically controlled HIV co-infection, treatment naïve/ interferon ± ribavirin experienced. Non-injecting drug users, including participants compliant in opioid substitution maintenance programmes.

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

Treatment and monitoring

- 12 or 24 weeks of once-daily ravidasvir 200 mg + sofosbuvir 400 mg
- Clinical and laboratory assessments at weeks 1 and 4 and then every 4 weeks during treatment and at 4-, 12-, and 24-weeks post-treatment.



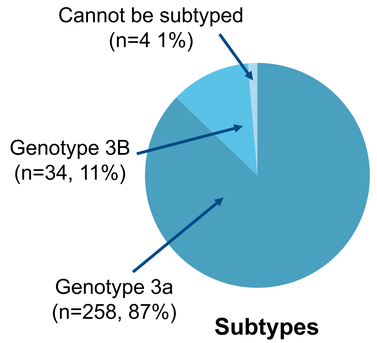
Results

Of the total 603 patients enrolled, 296 (49%) had HCV genotype 3. Overall SVR at 12 & 24 weeks post-treatment (SVR12/24) =97.6% (289/296)

Three patients who did not achieve SVR12/SVR24 discontinued treatment early after 2, 3 and 9 doses of study drugs.

Four patients (4/296, 1.4%) had virological failure:

- Three had baseline resistance-associated substitution (RAS), 93H (n = 2) and 30K+31M (n = 1)
- One patient had no baseline RAS results as amplification was not possible
- None had treatment-emergent RAS in NS5A or NS5B.

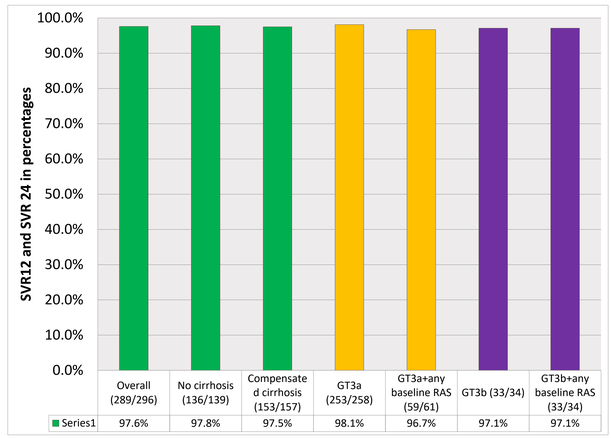


Baseline characteristics of study participants

	All patients with GT 3 (N=296*) n (%) or median(IQR)	GT3 without cirrhosis (N=139*) n (%) or median (IQR)	GT3 with compensated cirrhosis (N=157*) n (%) or median (IQR)
Male	227 (77%)	103 (74%)	124 (79%)
Age (years)	48 (41-56)	44 (36-52)	51 (44-58)
BMI (kg/m^2)	24.2 (21.5-27.0)	22.7 (20.9-25.3)	25.1 (22.8-28.2)
Previous IFN±RBV	68 (23%)	37 (27%)	31 (20%)
Patient reported past IDU	146 (49%)	70 (50%)	76 (48%)
Co-morbidities			
Diabetes mellitus	42 (14%)	15 (11%)	27 (17%)
Hypertension	78 (26%)	26 (19%)	52 (33%)
Dyslipidemia	12 (4%)	4 (3%)	8 (5%)
Fatty liver	18 (6%)	7 (5%)	11 (7%)
HIV co-infection	67 (23%)	41 (29%)	26 (17%)
Platelets (x10^9/L)	184 (138-229)	211 (174-254)	158 (112-202)
Alanine transaminase (U/L)	82 (52-119)	64 (39-107)	93 (63-137)
Asparate transaminase (U/L)	65 (46-94)	50 (35-68)	81 (61-113)
Albumin (g/L)	41 (39-44)	42 (40-45)	40 (38-42)
Total bilirubin (umol/L)	12 (9-17)	10 (7-13)	14 (11-20)
Creatinine (umol/L)	74 (64-86)	78 (64-89)	72 (63-81)
Liver stiffness (kPa)	N=293 13.4 (6.9-20.3)	N=137 6.8 (5.6-8.8)	N=156 19.4 (15.8-27.0)
APRI	1.1 (0.6-1.8)	0.6 (0.5-1.1)	1.4 (1.0-2.6)
HCV RNA ($\log_{10}$ IU/mL)	6.2 (5.6-6.7)	6.2 (5.5-6.7)	6.1 (5.7-6.6)
HCV Subtypes 3a/ 3b/ cannot be subtyped	258 (87%)/ 34 (11%)/ 4 (1%)	118 (85%) /18 (13%) / 3 (2%)	140 (89%)/ 16 (10%)/ 1 (1%)

*Unless otherwise specified.

Sustained Virological Response at 12 and 24 weeks (SVR12&24)



Of the 41 patients with GT3a and baseline Y93H RAS, 39 (95.1%) achieved SVR12/24, including all 9 patients with both S62L and Y93H RAS.

Conclusions

- In patients with chronic GT3 hepatitis C, this ravidasvir and sofosbuvir combination achieved high SVR12/24 of 97.8% and 97.5% when given to patients for 12 weeks (patients without cirrhosis) and 24 weeks (patients with compensated cirrhosis), respectively.
- There was no evidence of treatment-emergent virologic resistance and the presence of Y93H RAS at baseline had a minimal impact on response rates

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