Advances in Chronic Hepatits C Management and Treatment

REPORTING ON EASL 2015

Comprehensive Expert Review and Discussion of Key Presentations

SAFETY AND EFFICACY OF SHORT-DURATION TREATMENT WITH GS-9857 COMBINED WITH SOFOSBUVIR/GS-5816 IN TREATMENT-NAÏVE AND DAA-EXPERIENCED GENOTYPE 1 PATIENTS WITH AND WITHOUT CIRRHOSIS

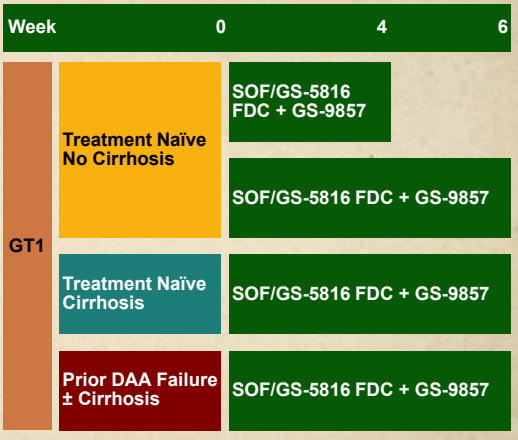
E.J. Gane, R.H. Hyland, Y. Ying, E. Svarovskaia, L.M. Stamm, D.M. Brainard, G.M. Subramanian, J.G. McHutchison, C. Schwabe

Abstract LP03

GS-9857 + SOF/GS-5816 in Treatment-Naïve and DAA-Experienced Patients with GT 1 Infection ± Cirrhosis

- Sofosbuvir (SOF)
  - Potent antiviral activity against HCV GT 1-6
  - Once-daily, oral, 400mg tablet
- GS-5816
  - Picomolar potency against HCV GT 1-6
  - 2nd generation NS5A inhibitor with improved resistance profile
- SOF/GS-5816 FDC
  - Once daily, oral, fixed-dose (400/100 mg) combination for HCV infection
- GS-9857
  - HCV NS3/4A protease inhibitor with potent antiviral activity against HCV GT 1-6
  - Improved resistance profile compared with other HCV protease inhibitors

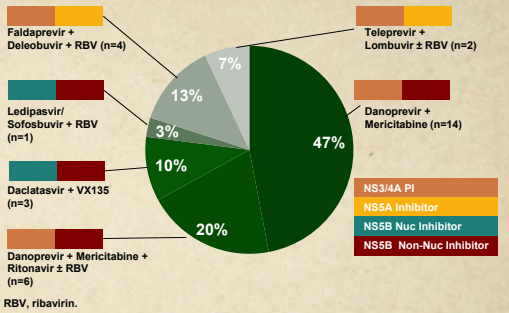
Study Design



Gane E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP03.

Baseline Characteristics and Prior DAA Treatment Failure Group

	SOF/GS-5816 FDC + GS-9857			
	4 Weeks	6 Weeks	6 Weeks	6 Weeks
	Treatment Naïve No Cirrhosis n=15	Treatment Naïve No Cirrhosis n=15	Treatment Naïve Cirrhosis n=15	Prior DAA Failure ± Cirrhosis n=30
Mean age, y (range)	54 (40-64)	50 (24-65)	59 (51-66)	55 (35-73)
Male, n (%)	9 (60)	7 (47)	11 (73)	24 (80)
White, n (%)	12 (80)	14 (93)	14 (93)	27 (90)
Mean BMI, kg/m^2 (range)	27 (20-33)	25 (21-32)	27 (20-39)	27 (20-40)
IL28B CC, n (%)	5 (33)	5 (33)	8 (53)	6 (20)
Cirrhosis, n (%)	0	0	15 (100)	5 (17)
Mean HCV RNA, $\log_{10}$ IU/mL (range)	6.3 (5.2-7.1)	6.0 (4.4-6.7)	6.0 (3.9-7.1)	6.3 (5.2-7.4)
HCV GT 1a, n (%)	11 (73)	11 (73)	14 (93)	23 (77)
Treatment naïve, n (%)	15 (100)	15 (100)	15 (100)	0
DAA failures, n (%)	0	0	0	30 (100)

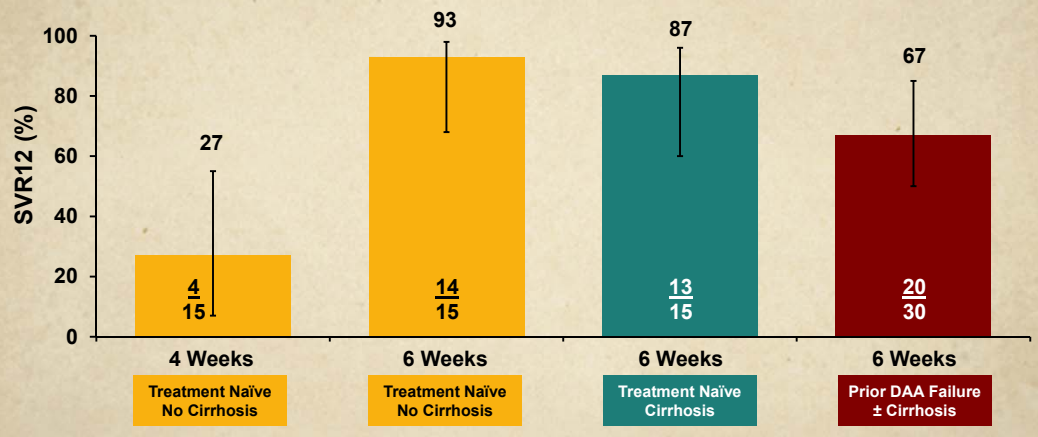


RBV, ribavirin.

Gane E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP03.

Gane: SOF/GS-5816 (2nd Gen NS5A Inhibitor) + GS-9857 (Protease Inhibitor): SVR12 in GT 1 Patients

- SVR12 Results (All failures due to relapse)



Gane E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP03.

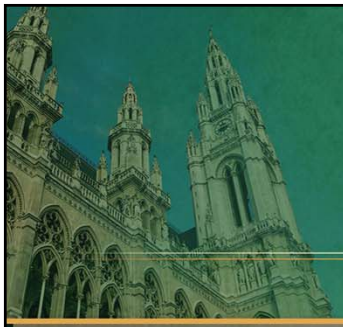
RAVs Were not Detected in Most Patients with Relapse Following Short Triple Therapy

- Resistance selection in patients with relapse (n=24)

		SOF/GS-5816 FDC + GS-9857			
		4 Weeks	6 Weeks	6 Weeks	6 Weeks
		Treatment Naïve No Cirrhosis n=11	Treatment Naïve No Cirrhosis n=1	Treatment Naïve Cirrhosis n=2	Prior DAA Failure ± Cirrhosis n=10
NS3	With sequence data at relapse, n	10*	0*	2	3*
	Selected RAVs, n/n	0/10	N/A	1/2 †	0/3
NS5A	With sequence data at relapse, n	10*	0*	2	3*
	Selected RAVs, n/n	0/10	N/A	0/2	0/3
NS5B	With sequence data at relapse, n	10*	1	2	3*
	Selected RAVs or TEVs, n/n	0/10	0/1	0/2	0/3

* Sequencing is ongoing. †Low level of V55A (1.9%) was detected.

Gane E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP03.



Advances in Chronic Hepatits C Management and Treatment

REPORTING ON EASL 2015

Comprehensive Expert Review and Discussion of Key Presentations

HIGH EFFICACY OF RETREATMENT WITH LEDPASVIR AND SOFOSBUVIR IN HCV PATIENTS WHO FAILED INITIAL SHORT COURSE THERAPY WITH COMBINATION DAA REGIMENS (NIH) SYNERGY TRIAL

E.M.P. Wilson, S. Kattakuzhy, Z. Sims, L. Tang, M. McLaughlin, A. Price, R. Silk, C. Gross, E. Akoth, A. Osinusi, H. Masur

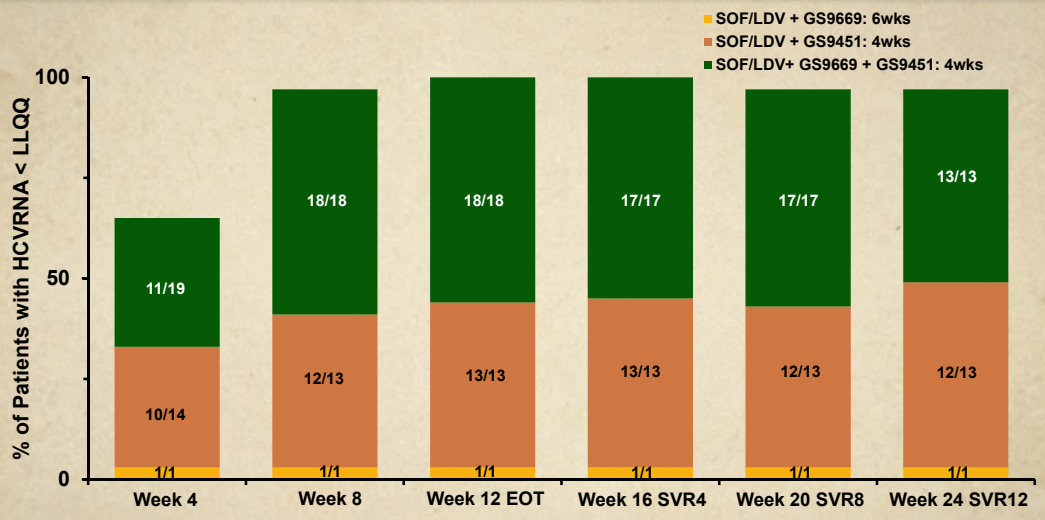
Abstract LP09

Retreatment with LDV/SOF in Patients Who Failed Initial Short Course Treatment in the SYNERGY Trial

	N = 34
Age, years, mean ± SD	59.5 ± 6.8
Sex	
Male, n (%)	28 (82.3)
Female, n (%)	6 (17.7)
Race	
Black, n (%)	29 (85.3)
White, n (%)	5 14.7)
HCV Genotype	
1a, n (%)	26 (76.4)
1b, n (%)	8 (23.6)
BMI, kg/m^2, mean ± SD	27.5 ± 3.7
HCV RNA, >800,000 IU/mL, n (%)	22 (64.7)
Liver Fibrosis	
0-2, n (%)	33 (97.1)
3, n (%)	1 (2.9)
Weeks to retreatment, mean ± SD	21.5 ± 8.0
Resistance –associated variants, >20 resistance	
NS5A, n (%)	22 (64.7)
NS5B, n (%)	1 (2.9)
NS5A and NS5B, n (%)	1 (2.9)

Wilso E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP09.

Retreatment with LDV/SOF in Patients Who Failed Initial Short Course Treatment in the SYNERGY Trial



Data collection is ongoing, but we report SVR4 rates of 94% (31/33; ITT) and 100% (31/31, per protocol) and SVR12 rates of 89.6% (26/29; ITT) and 96.3% (26/27; per protocol), with one patient experiencing virologic rebound 8 weeks after completion of therapy, one patient lost to follow up, and one patient withdrawing consent after week 4. For SVR rates by original treatement group in a per protocol analysis, fee Figure.

Wilso E, et al. 50th EASL; Vienna, Austria; April 22-26, 2015. Abst. LP09.