SIMEPREVIR (TMC435) WITH PEGINTERFERON/RIBAVIRIN FOR TREATMENT OF CHRONIC HCV GENOTYPE 1 INFECTION IN EUROPEAN PATIENTS WHO RELAPSED AFTER PREVIOUS INTERFERON-BASED THERAPY: THE PROMISE TRIAL

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Background/aims: Simeprevir (SMV) is a one pill, once-daily (QD), oral HCV NS3/4A protease inhibitor. PROMISE was a randomised, double-blind, Phase III trial evaluating SMV plus peginterferon α-2a/ribavirin (PR) vs placebo (PBO)/PR in genotype (GT)1 HCV patients who relapsed after previous interferon-based therapy. Efficacy and safety data from PROMISE are presented for European patients. Methods: Patients received SMV 150mg QD (12wks) with PR (24 or 48wks; based on response-guided therapy), or PBO (12wks) plus PR (48wks). Patients were stratified by HCV GT1 subtype and *IL28B* GT. Primary efficacy endpoint: sustained virological response at 12wks (SVR12). Results: 274/393 (69.7%) patients were European (male 64.6%, white 97.8%, HCV GT1a/1b 29.2/70.4%, *IL28B* CC/CT/TT 22.6/65.3/12.0%, METAVIR F3/F4 14.7/14.0%); 18.5% of European HCV GT1a patients had Q80K. SVR12 was higher with SMV/PR versus PBO/PR in the European population overall and by patient sub-group [Table]. 173/184 SMV/PR patients (94.0%) were eligible for 24wks PR; 90.8% of these patients achieved SVR12. 81.5% of SMV/PR- and 3.4% of PBO/PR-treated patients achieved rapid virological response. On-treatment failure (3.3% vs 20.0%) and viral relapse rates (11.9% vs 43.5%) were lower with SMV/PR versus PBO/PR. In the SMV/PR arm (Wks1–12), most common AEs included fatigue, headache and influenza-like illness. Most were Grade 1/2 (Grade 3/4, 19.6%); no AEs resulted in SMV withdrawal. SAEs possibly related to SMV were infrequent (1.1%). No fatal AEs occurred. Conclusion: SMV confers clinical benefit and is generally well tolerated in European HCV GT1-infected patients.

Table: Rates of sustained virological response at 12wks (SVR12)

	SVR12, n/N (%)	
	SMV/PR	**PBO/PR**
All patients	206/260 (79.2*)	49/133 (36.8)
All European patients	161/184 (87.5*)	40/90 (44.4)
Patients who met RGT criteria	157/173 (90.8)	n/a
IL28B genotype CC	38/41 (92.7)	13/21 (61.9)
IL28B genotype CT	106/121 (87.6)	25/58 (43.1)
IL28B genotype TT	17/22 (77.3)	2/11 (18.2)
HCV GT 1a	52/59 (88.1)	8/22 (36.4)
HCV GT 1a with Q80K	6/8 (75.0)	4/7 (57.1)
HCV GT 1a without Q80K	45/50 (90.0)	4/15 (26.7)
HCV GT 1b	109/125 (87.2)	32/68 (47.1)
METAVIR score F0-F2	105/119 (88.2)	34/70 (48.6)
METAVIR score F3	26/30 (86.7)	2/9 (22.2)
METAVIR score F4	23/27 (85.2)	3/10 (30.0)

*p<0.001 vs PBO/PR; RGT, response-guided therapy

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