ONLINE EXPERT POSTER REVIEW AND DISCUSSION

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PSI-7977 PROTON and ELECTRON: 100% Concordance of SVR4 with SVR24 in HCV GT1, GT2 & GT3

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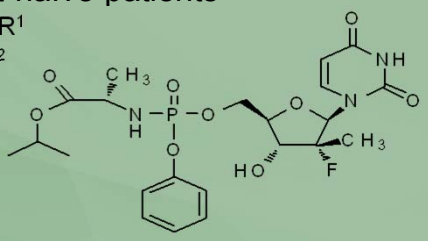
Abstract #7

Background

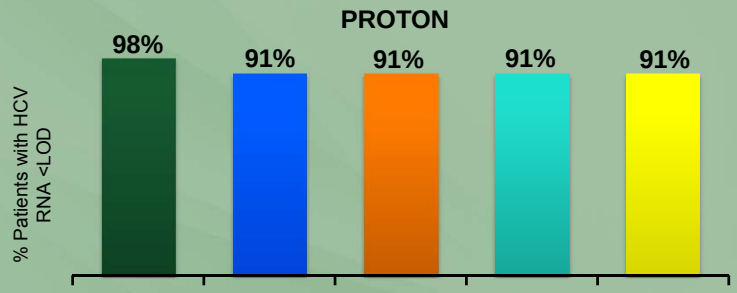
- GS-7977 (formerly PSI-7977) is a specific nucleotide analog inhibitor of HCV NS5B
- Safe and well-tolerated in clinical studies
- Once-daily, with or without food
- Potent antiviral activity with broad HCV genotype coverage with or without IFN in treatment-naïve patients
  - ELECTRON genotype 2/3: 100% SVR[1]
  - ELECTRON genotype 1: 100% RVR[2]
  - PROTON genotype 1: 91% SVR[3]
  - PROTON genotype 2/3: 94% SVR[4]
- High barrier to resistance



1Gane E, et al. AASLD 2011; 2Gane E, et al. CROI; 3Lawitz E, et al. AASLD 2011; 4Lalezari J, et al. EASL 2011.

Introduction

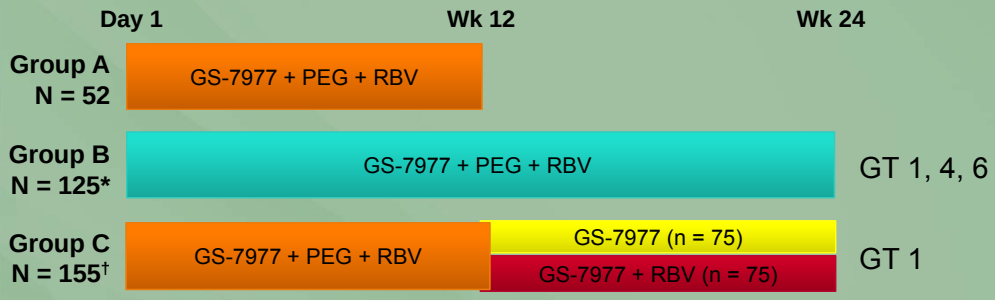
- GS-7977 400 mg + peginterferon (PEG) + ribavirin (RBV) provided 91% SVR in treatment-naïve patients with genotype 1 HCV infection (PROTON trial)
  - 24-week regimen: 12 weeks GS-7977/PEG/RBV + 12 weeks PEG/RBV



  - Given the high response rates, the next objective was to evaluate whether a total of 12 weeks of therapy could achieve the same results

Lawitz E, et al. AASLD, HepDart, 2011.

Atomic Study Design

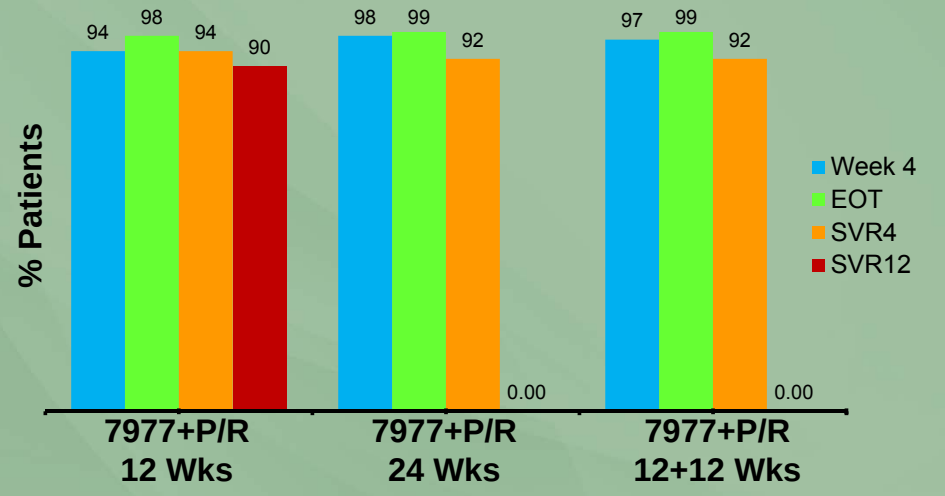


- Patients with HCV genotype 1 were randomized 1:2:3 into 1 of 3 open-label arms
- Stratified by:
  - IL28B genotype (CC vs non-CC)
  - HCV RNA at screening (≤ vs >800,000 IU/mL)
- HCV RNA analyzed by TaqMan® HCV Test 2.0 (LOD: 15 IU/mL)

Kowdley K et al. 47th EASL; Barcelona, Spain; April 18-22, 2012. Abst. 1

*Of the 125 patients enrolled in Arm B, 16 were genotype 4 or 6
†5 of the 155 patients were not re-randomized at Week 12

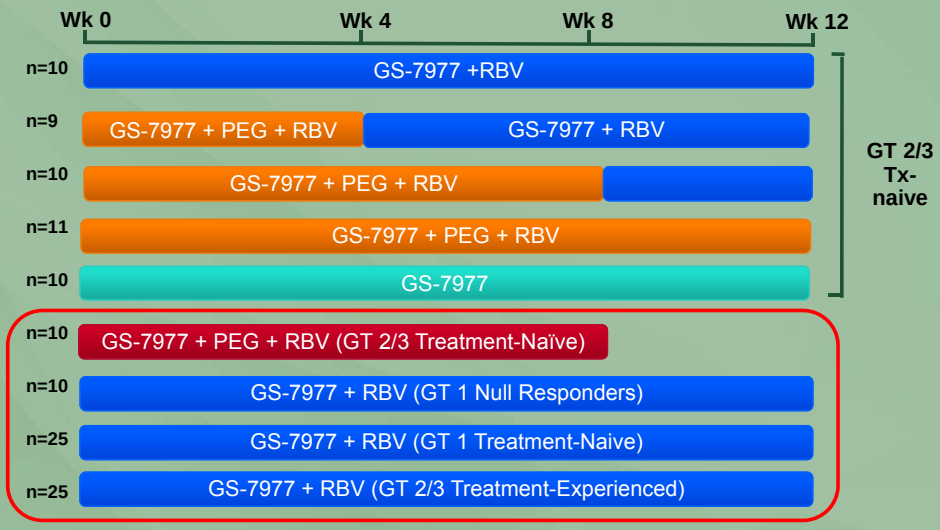
90% of Patients Achieved SVR12: GS-7977 + PEG/RBV 12-Week Regimen



- 94% of patients in Arm A who reached follow up Week 12 were <LOD

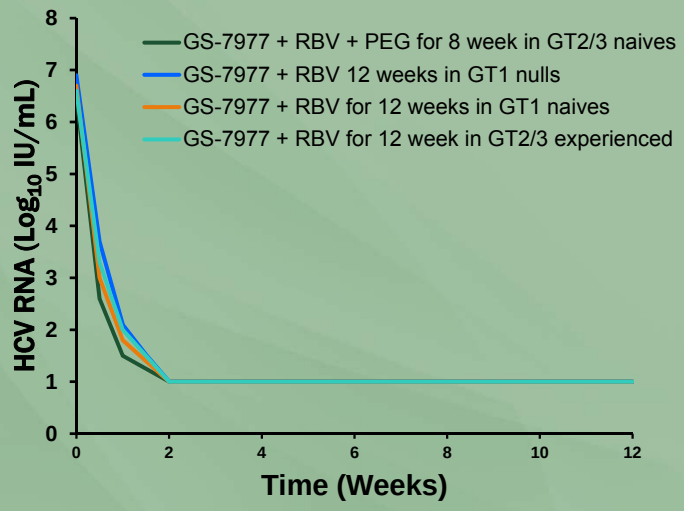
Kowdley K et al. 47th EASL; Barcelona, Spain; April 18-22, 2012. Abst. 1.

Electron Study Design



Gane E et al. 47th EASL; Barcelona, Spain; April 18-22, 2012. Abst. 1113.

On Treatment Viral Suppression



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Patients with HCV RNA <LOD Over Time n/N (%)

	GT 2/3 Treatment-naïve 8 wks (n=10)	GT 1 Null Responders 12 wks (n=10)	GT 1 Treatment-naïve 12 wks (n=25)	GT 2/3 Treatment-experienced 12 wks (n=25)
Week 1	6/10 (60)	1/10 (10)	8/24 (33)	8/25 (32)
Week 2	10/10 (100)	7/10 (70)	17/24 (71)	21/25 (84)
Week 4	10/10 (100)	10/10 (100)	25/25 (100)	25/25 (100)
EOT	10/10 (100)	9/9 (100)	25/25 (100)	21/21 (100)
SVR 4	10/10 (100)	1/9 (11)	25/25 (88)	12/15 (80)*
SVR 12	10/10 (100)	Quantum Per protocol 59% SVR 4		

* 1 subject relapsed at the SVR8 time point after having previously achieved SVR4

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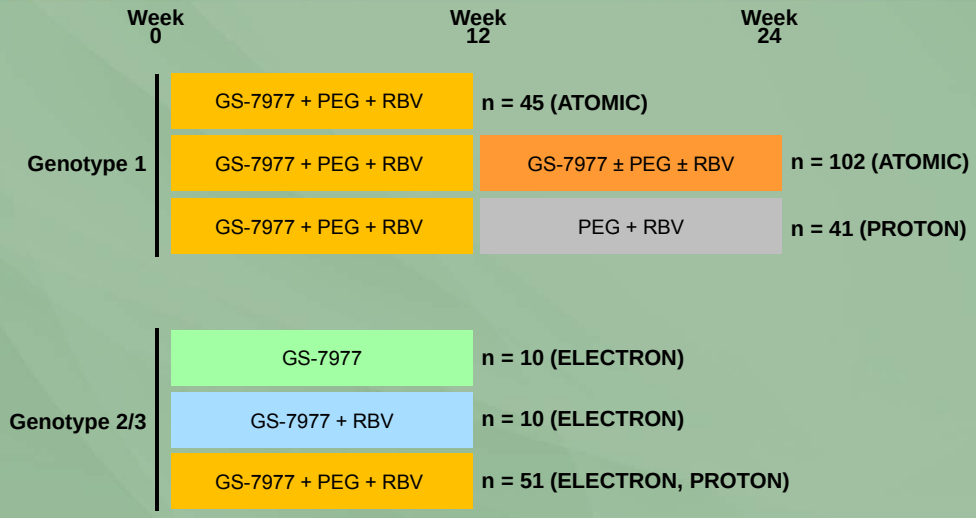
Patients Included in Analysis (N = 259)



Gane E et al. 47th EASL; Barcelona, Spain; April 18-22, 2012. Abst. 1113.

99%-100% Concordance

	Concordance of SVR4 with SVR12	Concordance of SVR4 with SVR24
All regimens	249/251 (99%)	107/107 (100%)
Regimens containing PEG	233/235 (99%)	91/91 (100%)
Regimens not containing PEG	16/16 (100%)	16/16 (100%)

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