Once Daily Sofosbuvir (GS-7977) Regimens in HCV Genotype 1-3: The ELECTRON Trial

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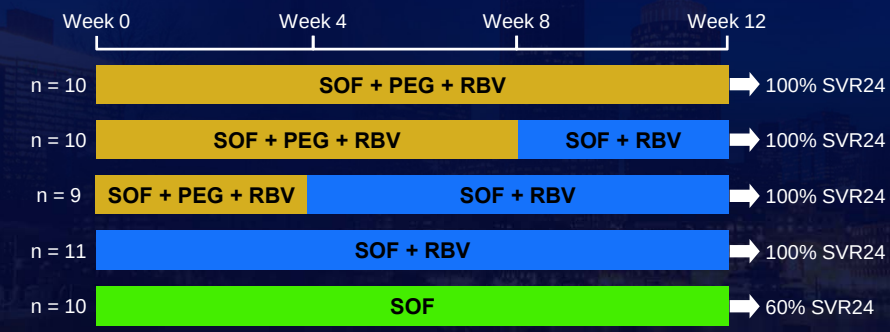
Abstract LB-1

ELECTRON: Genotype 2/3 Cohorts



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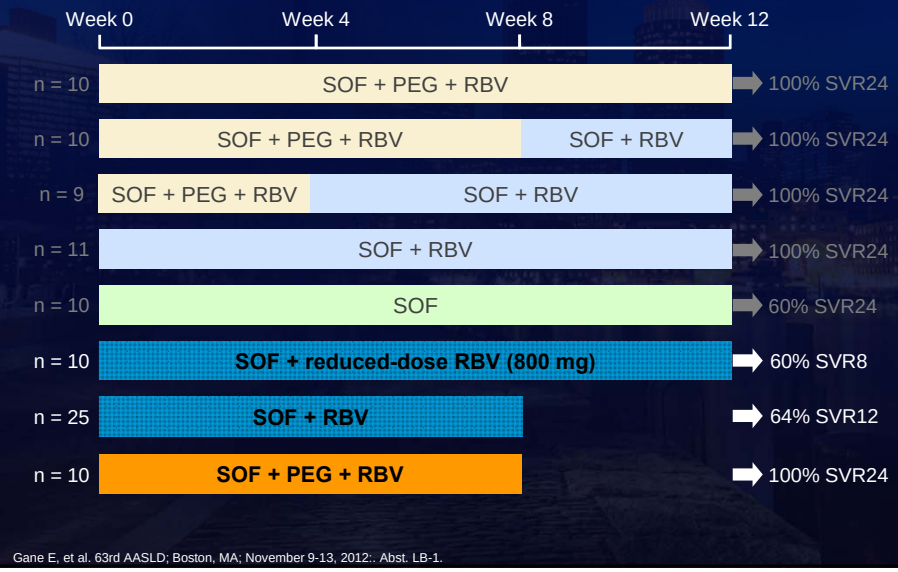

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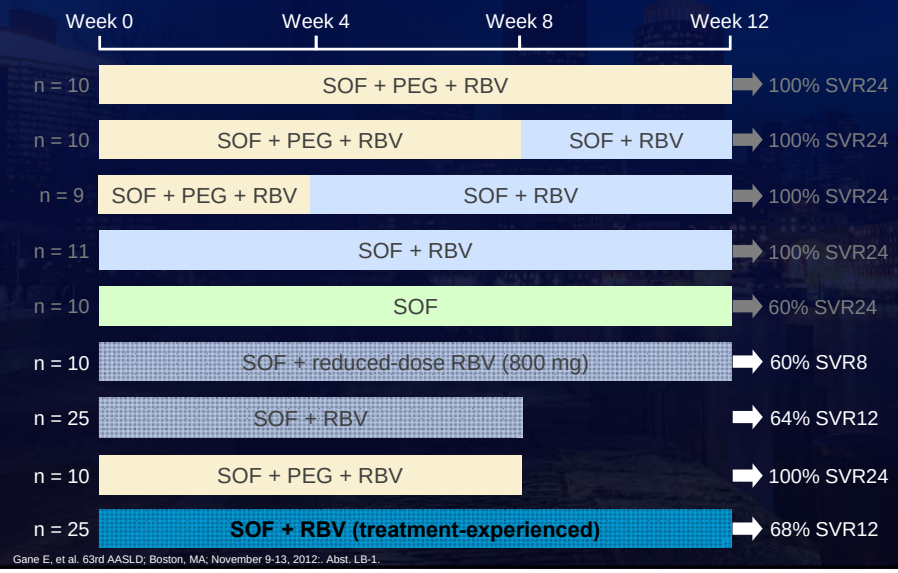

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Summary of Results in Genotype 2/3

- SOF combined with RBV for 12 weeks is associated with very high rates of SVR in patients infected with HCV genotype 2/3
- A reduced rate of SVR is associated with:
  - Lowered RBV dose (800 mg/day)
  - Shortened treatment duration (8 weeks)
  - Prior failure with PEG/RBV

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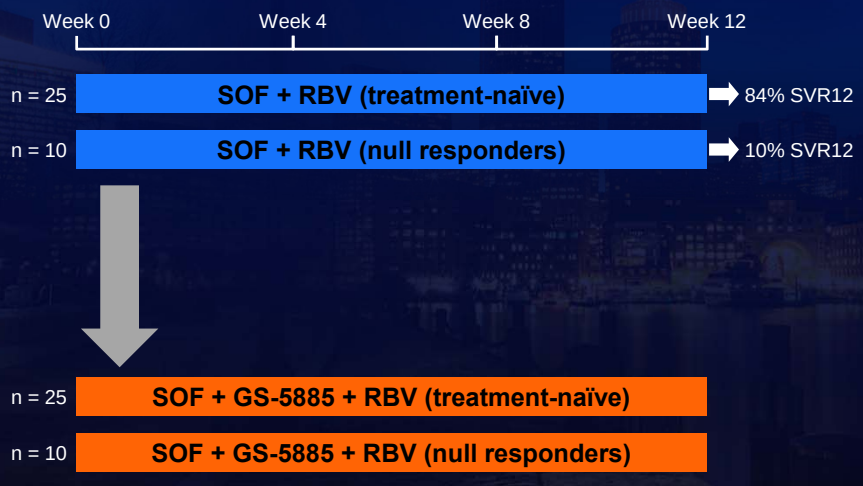
ELECTRON: Genotype 1 Cohorts



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Efficacy in Genotype 1 Patients

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

	SOF + RBV		SOF + GS-5885 + RBV	
	Treatment-naïve (n = 25)	Null responder (n = 10)	Treatment-naïve (n = 25)	Null responder (n = 9)
Week 1	8/25 (32)	1/10 (10)	11/25 (44)	0/9 (0)
Week 2	17/25 (68)	7/10 (70)	22/25 (88)	4/9 (44)
Week 4	25/25 (100)	10/10 (100)	25/25 (100)	8/9 (89)
EOT	25/25 (100)	10/10 (100)	25/25 (100)	9/9 (100)
SVR4	22/25 (88)	1/10 (10)	25/25 (100)*	3/3 (100)†
SVR12	21/25 (84)	1/10 (10)	--	--

HCV RNA analyzed by TaqMan® HCV Test 2.0 with limit of detection (LOD) of 15 IU/mL

*Includes one patient who stopped all treatment for SAE at week 8

†Data collection ongoing

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Adverse Events in Genotype 1 Patients

	SOF + RBV		SOF + GS-5885 + RBV	
	Treatment-naïve (n = 25)	Null responder (n = 10)	Treatment-naïve (n = 25)	Null responder (n = 9)
SAEs*	1 (4)	0	2 (8)	0
AEs that Led to Discontinuation	0	0	1 (4)†	0
≥Grade 2 AEs‡	10 (40)	3 (30)	12 (48)	2 (22)
Anemia	0	1 (10)	5 (20)	0
Headache	1 (4)	0	1 (4)	0
Depression	0	1 (10)	2 (8)	0
Ligament Sprain	1 (4)	1 (10)	0	0

*SAEs considered unrelated to SOF (urethral injury, pyelonephritis, enterovesical fistula + divertivulitis + diverticular perforation).

†Stopped all treatment at Week 8 at time of partial colectomy for diverticular perforation.

‡In more than 1 patient.

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Grade 3 and 4 Laboratory Abnormalities in Genotype 1 Patients

	SOF + RBV		SOF + GS-5885 + RBV	
	Treatment-naïve (n = 25)	Null responder (n = 10)	Treatment-naïve (n = 25)	Null responder (n = 9)
Grade 3	11 (44)	4 (40)	13 (52)	2 (22)
Grade 4	0	0	0	0
ALT	1 (4)	0	0	0
Total Bilirubin	1 (4)	0	0	0
Hemoglobin	3 (12)	3 (30)	5 (20)	2 (22)
Prothrombin Time	1 (4)	0	2 (8)	0
Urine Occult Blood*	5 (20)	2 (20)	9 (36)	0

- *Majority of occult blood findings unconfirmed or in females

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Summary: Sofosbuvir in HCV Genotype 1

- 12 weeks SOF + RBV provided SVR12 in 84% of treatment-naïve, but only in 10% of null responders
- Addition of GS-5885 increased efficacy of SOF + RBV
  - 100% SVR4 in treatment-naïve patients
  - No impact of HCV genotype subtype, IL28B status, BMI
  - No additional safety or tolerability issues detected
  - No virologic failures

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Conclusions

- In HCV genotype 2 or 3 infection, sofosbuvir + RBV for 12 weeks appears to be a safe and effective regimen for both treatment-naïve and previously treated patients
  - Durations of less than 12 weeks or reduced RBV dose may adversely impact treatment efficacy
- In HCV genotype 1 infection, sofosbuvir + GS-5885 + RBV for 12 weeks appears to be a safe and effective regimen for treatment-naïve patients
  - Awaiting full results in prior null responders

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