Concordance Between SVR4, SVR12, and SVR24 in HCV-Infected Patients Who Received Fixed-Dose Combination Sofosbuvir/Velpatasvir in Phase 3 Clinical Trials

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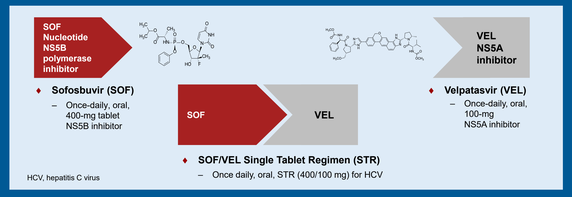
INTRODUCTION



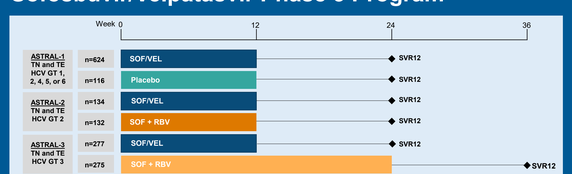
- The SOF/VEL Phase 3 ASTRAL-1, -2, and -3 program evaluated SOF/VEL in treatment-naïve (TN) and treatment-experienced (TE) patients both with and without compensated cirrhosis.
- SOF/VEL has been shown to be safe and effective (sustained virologic response 12 weeks after treatment completion [SVR12] >90%) in TN and TE patients, and was the first pangenotypic single-tablet regimen for the treatment of chronic HCV.[1-2]
- As HCV treatment expands to resource limited populations or beyond tertiary care, simplistic algorithms require clarification on when SVR can be determined. SVR concordance with SOF/VEL supports this shift to a minimal monitoring strategy.[3]

OBJECTIVE

To evaluate the concordance of SVR 4 weeks after treatment completion (SVR4) with SVR12, and SVR12 with SVR 24 weeks after treatment completion (SVR24) in patients receiving SOF/VEL in the Phase 3 ASTRAL-1 (GS-US-342-1138; NCT02201940), ASTRAL-2 (GS-US-342-1139; NCT02220998), and ASTRAL-3 (GS-US-342-1140; NCT02201953) studies.

METHODS

Sofosbuvir/Velpatasvir Phase 3 Program



Total Patients in ASTARL-1, -2, and -3: n=1558
Total Patients on SOF/VEL alone: n=1035

- HCV RNA data from patients in ASTRAL-1, ASTRAL-2, and ASTRAL-3 were evaluated.
- SVR was defined as patients with HCV RNA < lower limit of quantitation (15 IU/mL) at the aforementioned post-treatment visits, using the COBAS® TaqMan® HCV Test v2.0.
- Only patients with both SVR4 and SVR12 or SVR12 and SVR24 data were included in this concordance analysis.
- No data were imputed.

RESULTS

Demographics: Phase 3 ASTRAL Studies

	Total, N=1558	SOF/VEL, N=1035
Mean age, y	53	53
Men, n (%)	944 (61)	630 (61)
Black, n (%)	85 (6)	61 (6)
Hispanic, n (%)	107 (7)	68 (7)
Mean BMI, kg/m² (SD)	26.9	26.8
HCV GT 1/2/3/4/5/6, n (%)	393(25)/391(25)/552(35)/ 138 (9)/25(2)/49(3)	328(32)/238(23)/277(27)/ 116(11)/35(3)/41(4)
Mean baseline HCV RNA, log_{10} IU/mL (SD)	6.3 (0.70)	6.3 (0.70)
Cirrhosis, n (%)	343 (22)	220 (21)
Treatment-experienced, n (%)	415 (27)	291 (28)

SVR4 and SVR12 Concordance

		SVR12, n	
		Yes	No
SVR4	Yes	1002	3
	No	0	10

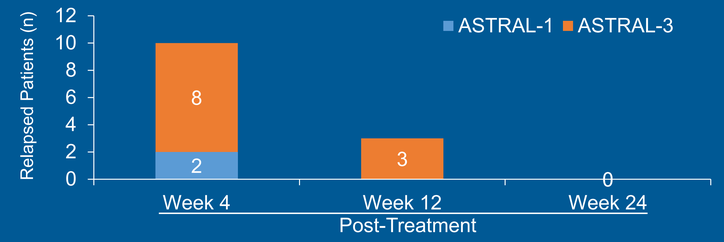
- 99.7% positive predictive value
- 100% negative predictive value

SVR12 and SVR24 Concordance

		SVR24, n	
		Yes	No
SVR12	Yes	991	0
	No	0	2

- 100% positive predictive value
- 100% negative predictive value

Timing of Viral Relapse or Reinfection



Patient Details on Viral Relapse or Reinfection

Patient #	GT	SVR4	SVR 12	SVR 24	Relapsed	Previous Regimen	Cirrhosis	Previous Outcome
1	3a	Yes	No	No	Between SVR4 & SVR12	PEG + RBV	Yes	Nonresponder
2	3a	Yes	No	No	Between SVR4 & SVR12	None (TN)	Yes	N/A
3	3a	Yes	No	No	Between SVR4 & SVR12	PEG +RBV	No	Relapse/breakthrough
4	1a	No	No	No	Before SVR4	None (TN)	No	N/A
5	1b	No	No	No	Before SVR4	PEG + RBV	Yes	Nonresponder
6	3a	No	No	No	Before SVR4	None (TN)	Yes	N/A
7	3a	No	No	No	Before SVR4	PEG + RBV	No	Relapse/breakthrough
8	3a	No	No	No	Before SVR4	None (TN)	No	N/A
9	3a	No	No	No	Before SVR4	PEG + RBV	Yes	Relapse/breakthrough
10	3	No	No	No	Before SVR4	PEG +RBV	No	Relapse/breakthrough
11	3a	No	No	No	Before SVR4	PEG+RBV	Yes	Nonresponder
12	3a	No	No	No	Before SVR4	None (TN)	Yes	N/A
13	3a	No	No	No	Before SVR4	PEG+RBV	Yes	Nonresponder

RESULTS

- There were 20 patients from ASTRAL-1, -2, and -3 who received SOF/VEL (n=1015/1035) and did not achieve SVR12
  - 13 patients who experienced virologic relapse or reinfection
  - 4 lost to follow-up
  - 1 discontinuation of drug
  - 1 withdrew consent
  - 1 death – unrelated to treatment
- Of 13 patients who relapsed or reinfected, 10 occurred at post-treatment Week4, and 3 occurred at post-treatment Week 12:
  - 2 were GT1; 11 were GT3
  - 8 had compensated cirrhosis
  - 8 had been previously been treated with peg-interferon + ribavirin
- There was 1 GT3a patient with confirmed GT1a reinfection between post-treatment Week 4 and post-treatment Week 12
  - This would potentially change the PPV for SVR4 and SVR12 concordance from 99.7% to 99.8%.

CONCLUSIONS

- For SOF/VEL, there was high concordance (99.7% positive predictive value) between SVR4 and SVR12.
  - 3 of 1025 patients (0.3%) who achieved SVR4 subsequently did not achieve SVR12. All were GT3a.
  - The 1 GT1a reinfected patient would potentially change the PPV from 99.7% to 99.8%.
- There was 100% concordance between SVR12 and SVR24.
- These results suggest SVR4 may be utilized to predict long-term SVR, as opposed to SVR12 and SVR24. This approach could be valuable in patients with high risk (PWID or incarcerated individuals released) of not attending SVR12 assessment.
- This data supports alternative approaches to SVR assessment. In addition, this supports EASL guidance that testing for SVR can be omitted in certain patients.

REFERENCES: 1. Feld JJ et al. N. Engl J Med 2015; 373: 2599-2607; 2. Foster GR et al. N. Engl J Med 2015; 373: 2608-2617; 3. Solomon S et al. AASLD 2020 LO7.

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