Curing Hepatitis C Virus (HCV) with Direct-Acting Antiviral (DAA) Treatment: Adherence and Rapid Onset of HCV RNA Undetectability After 4 Weeks of Treatment with Sofosbuvir/Velpatasvir

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Conclusions

SOF/VEL achieved rapid viral load reduction below LLOQ in >90% of patients after only 4 weeks of treatment and 99.9% at week 12.

More than 95% of patients demonstrated >80% adherence to treatment. Patients whose adherence was <80% were less likely to achieve SVR12 (78%).

With SOF/VEL combination, without RBV, almost 100% of SVR can be achieved provided a patient is taking the medication.

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. Lancet Gastroenterol & Hepatol 2022;7(4):307-317; 4.Sowah L et al. CROI 2022, Poster 530

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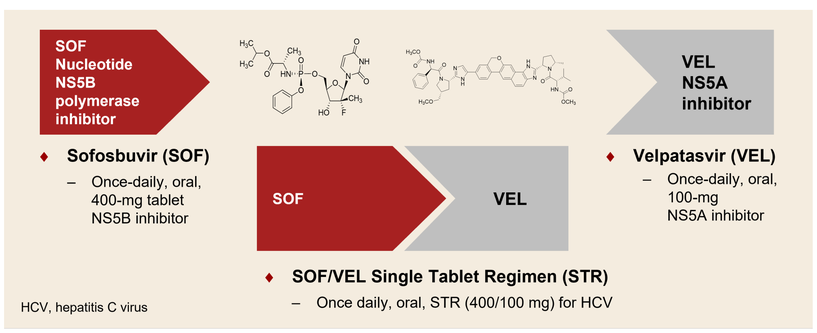
Introduction



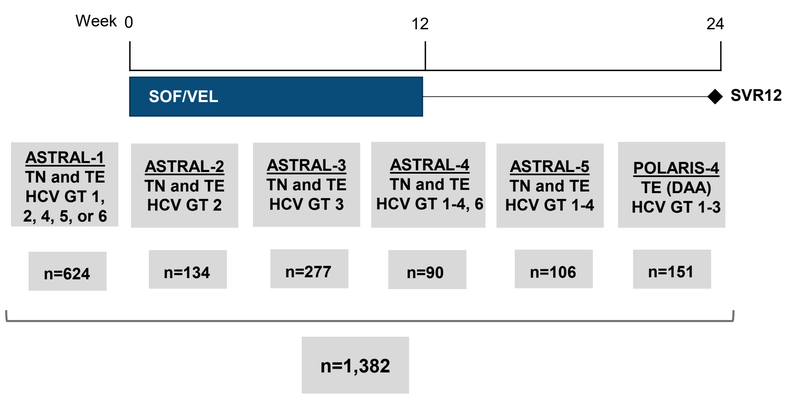
- Sofosbuvir/Velpatasvir (SOF/VEL) has been extensively evaluated in Phase 3 randomized clinical trials (RCTs) in treatment-naïve (TN) and treatment-experienced (TE) patients both with and without compensated cirrhosis.[1-2]
- SOF/VEL 12 weeks without ribavirin (RBV) has been shown to be safe and effective (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]
- Recently the MinMon (minimal monitoring approach) study[3-4] described that self-reported adherence during the first 4 weeks of SOF/VEL was associated with achieving high SVR rates.

Objective

- We aimed to explore viral suppression during SOF/VEL treatment (without RBV), linking the adherence component with the on-treatment rate of HCV RNA undetectability over the 12 weeks of treatment.

Methods

SOF/VEL Without RBV in Phase 3 RCTs



- This post-hoc analysis of Phase 3 trials with SOF/VEL 12 weeks without RBV included six RCTs (ASTRAL 1 to 5, and POLARIS 4).
- We captured patient characteristics, and proportion of patients with HCV RNA less than the lower limit of quantification (LLOQ) while on treatment (Weeks 2, 4, 8 and 12). The LLOQ used during clinical trials was 15 IU/mL.
- Adherence was measured as pill-count at treatment visits by investigator or designee and was calculated to Day 84 except discontinuation due to virologic failure. Subjects who prematurely discontinue study drug for lack of efficacy (ie, virologic failure) had the total amount of study drug prescribed calculated up to the first date when virologic failure criteria were met.
- The proportion of patients reporting SOF/VEL adherence ≥80% and ≥90%, and the number of patients showing adherence <80% were evaluated. Adherence at week 4 was not available.
- SVR12 at each trial and the SVR12 linked to the 80% adherence cut-off (≥ and <) were also captured. The SVR12 was calculated as the weighted average for the Totals.

Results

Demographics

- A total of 1,382 patients treated with SOF/VEL without RBV were included in the analysis of the six Phase 3 trials (Table 1).
- Mean age was 54 (+3.3SD) years old, being male 65%, GT3 26%, cirrhotic 29%, and decompensated 7% of the total population, representing 29% of the cirrhotic population (Table 1).

Onset in HCV RNA Undetectability

- Undetectable HCV RNA was obtained at week 2 in 57.2% of patients, at week 4 in 90.3%, at week 8 in 99.6%, and at week 12 in 99.9% (Table 2).
- Among the clinical trial cohorts, patients with decompensated cirrhosis treated with SOF/VEL without RBV had the lowest HCV RNA undetectable proportion at week 4 (81.1%) (ASTRAL 4; Table 2).

Adherence

- The proportion of patients reporting adherence was high:
  - ≥80% adherence in 95.5% of patients
  - ≥90% adherence in 95.1% of patients
- In the overall population (N=1,382), only 64 patients (4.6%) showed an adherence <80% (Table 3).

Results

SVR12

- The weighted average for the total SVR12 obtained by SOF/VEL without RBV in the six clinical trials was 96% (Table 4). Coincident with HCV RNA undetectability at week 4, the lowest SVR12 was achieved in patients with decompensated patients (ASTRAL 4; 83.3%).
- The SVR12 linked to an adherence ≥80% was of 97.6%.
- Only 64 patients had a reported adherence <80%, the average SVR12 was 78.1% with a wide range of response [28.6 to 92.3]. The decompensated patients were the most impacted by the decreased in adherence (Table 4)

A Summary Table is provided selecting key variables for each clinical trial and overall.

Summary Table: Clinical Trials with Sample Sizes, Proportion of Patients Achieving HCV RNA Less than LLOQ While On Treatment (W2, W4, W8, W12), Adherence Rate ≥80% and SVR12 Linked to That Adherence

Trial	N	Week 2	Week 4	Week 8	Week 12	Adherence ≥80%	SVR with adherence ≥80%
ASTRAL 1	624	56.9%	**90.5%**	99.7%	100%	96.5%	99.3%
ASTRAL 2	134	57.1%	**90.2%**	100%	100%	97.0%	100%
ASTRAL 3	277	62.0%	**91.7%**	99.6%	100%	95.3%	95.5%
ASTRAL 4*	90	34.4%	**81.1%**	98.9%	100%	92.2%	86.7%
ASTRAL 5**	106	68.0%	**92.2%**	100%	100%	91.5%	97.9%
POLARIS 4$	151	56.0%	**91.0%**	99.0%	99.0%	95.1%	98.3%
TOTAL#	1,382	57.2%	**90.3%**	99.6%	99.9%	95.5%	97.6%

* ASTRAL4 consisted of decompensated patients treated with SOF/VEL 12 weeks without RBV. Decompensation was classified as Child–Pugh–Turcotte (CPT) class B (a score of 7 to 9 on a scale ranging from 5 to 15); ** ASTRAL5 included HIV/HCV coinfected patients; $ POLARIS4 consisted of DAA-experienced patients; # Weighted average for the Totals

Table 1: Demographics

Trial	N	Age (mean)	Male (%)	Cirrhotic (%)	Decomp* (%)	GT3 (%)
ASTRAL 1	624	54	60	19	0	0
ASTRAL 2	134	57	64	14	0	0
ASTRAL 3	277	49	61	29	0	100
ASTRAL 4	90	58	63	100	100	16
ASTRAL 5	106	54	86	18	0	11
POLARIS 4	151	57	76	46	0	34
TOTAL	*1,382*	*54*	*65*	*29*	*7*	*26*

*Decompensated cirrhosis was classified as Child–Pugh–Turcotte (CPT) class B (a score of 7 to 9 on a scale ranging from 5 to 15)

Table 2: HCV RNA Undetectability (% of Patients)

Trial	N	Week 2	Week 4	Week 8	Week 12
ASTRAL 1	624	56.9	**90.5%**	99.7%	100%
ASTRAL 2	134	57.1	**90.2%**	100%	100%
ASTRAL 3	277	62.0	**91.7%**	99.6%	100%
ASTRAL 4	90	34.4	**81.1%**	98.9%	100%
ASTRAL 5	106	68.0	**92.2%**	100%	100%
POLARIS 4	151	56.0	**91.0%**	99.0%	99.0%
TOTAL	*1,382*	*57.2*	***90.3%***	*99.6%*	*99.9%*

Table 3: Adherence (% of Patients and # of Patients)

Trial	N	Adherence ≥90% (%)	Adherence ≥80% (%)	# patients with <80% adherence
ASTRAL 1	624	96.3	96.5	22
ASTRAL 2	134	96.3	97.0	4
ASTRAL 3	277	94.6	95.3	13
ASTRAL 4	90	92.2	92.2	7
ASTRAL 5	106	89.6	91.5	9
POLARIS 4	151	95.1	95.1	9
TOTAL	*1,382*	*95.1*	*95.5*	*64*

Table 4: SVR12 (%) In All Patients, and Depending on Adherence Cut-off

Trial	N	SVR12 (all)	SVR in adh ≥80%	SVR in adh <80%
ASTRAL 1	624	99.0	99.3	90.9
ASTRAL 2	134	99.3	100	75.0
ASTRAL 3	277	95.3	95.5	92.3
ASTRAL 4	90	83.3	86.7	28.6
ASTRAL 5	106	95.3	97.9	66.7
POLARIS 4	151	90.1	98.3	77.8
TOTAL	*1,382*	*96.0*	*97.6*	*78.1*