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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Background: Recently the MINMON (minimal monitoring approach) study described that self-reported adherence during the first 4 weeks of sofosbuvir/velpatasvir (SOF/VEL) was associated with achieving sustained virologic response (SVR). We aimed to explore viral suppression during the DAA treatment, linking the adherence component with the on-treatment rate of HCV RNA undetectability over the 12 weeks of treatment.

Methods: This post-hoc analysis of Phase 3 trials with SOF/VEL 12 weeks without ribavirin (RBV) (ASTRAL 1-5, and POLARIS 4) 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 of 15 IU/mL. The proportion of patients reporting SOF/VEL adherence ≥80% and SVR12 linked to this adherence cut-off were also captured.

Results: A total of 1,382 patients were included in the analysis: Mean age 54 (+3.3SD) years old, male 64.5%, GT3 25.6%, cirrhotic 28.8% (decompensated 29.2% of cirrhotic population). 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). 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%). The proportion of patients reporting adherence ≥80% was 95.5%, and SVR12 linked to that adherence was 97.6%.

Conclusion: Patients were highly adherent to treatment and SOF/VEL 12 weeks without RBV achieved rapid viral load reduction below LLOQ in >90% of patients after only 4 weeks of treatment and in 99.9% of patients at week 12.

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 adhe ≥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; ** ASTRAL5 included HIV/HCV coinfected patients; [$] POLARIS4 consisted of DAA-experienced patients; [#] Weighted average for the Totals.