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# Efficacy And Safety of Sofosbuvir/Velpatasvir in Patients With Chronic Hepatitis C Virus Infection Receiving Opioid Substitution Therapy: Analysis of Phase 3 ASTRAL Trials


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## Introduction

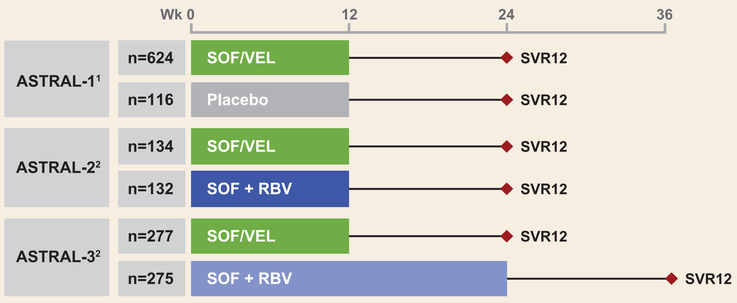
- The Phase 3 ASTRAL studies demonstrated that treatment with the once-daily fixed-dose combination tablet of sofosbuvir (SOF)/velpatasvir(VEL) was well tolerated and resulted in SVR12 rates >95% across all hepatitis C virus (HCV) genotypes[1-3]
- HCV infection is highly prevalent in patients with history of injection drug use, including those receiving opioid substitution therapy (OST)
- Neither SOF nor VEL has significant drug–drug interactions with medications commonly used for OST and, therefore, patients on OST were not excluded from the ASTRAL clinical program

## Objectives

- To perform a retrospective analysis to compare safety, efficacy, and adherence with SOF/VEL treatment in patients receiving or not receiving OST

## Methods

### ASTRAL Study Designs




- A retrospective analysis was performed using data from SOF/VELtreated patients in ASTRAL-1, -2, and -3 (ClinicalTrials.gov NCT02201940, NCT02220998, and NCT02201953, respectively)
- Records of concomitant medications reviewed for use of OST (including methadone, buprenorphine)
- People with clinically relevant illicit drug use within 12 months or a positive urine drug screen at screening were excluded. No drug screens were performed during or following treatment.
- Frequency and severity of treatment-emergent adverse events (AEs) and laboratory abnormalities compared between SOF/VEL-treated patients on and not on OST
- Virologic outcomes (SVR12, virologic failure) calculated for patients on and not on OST
- Adherence to SOF/VEL calculated using pill count at every visit for patients on and not on OST
- Deep sequencing of HCV NS5A/NS5B was performed for all patients at baseline and at virologic failure to distinguish viral relapse from reinfection

## Results

### Demographics

| | OST n=51 | Non-OST n=984 |
|---|---|---|
| Mean age, y (SD) | 49 (10) | 53 (11) |
| Male, n (%) | 39 (76) | 591 (60) |
| Race, n (%) | | |
| White | 46 (90) | 821 (83) |
| Black | 1 (2) | 60 (6) |
| Mean BMI, kg/m$^2$ (range) | 26 (6) | 27 (5) |
| Cirrhosis, n (%) | 11 (22) | 208 (28) |
| Treatment experienced, n (%) | 11 (22) | 280 (28) |
| IL28B CC, n (%) | 23 (45) | 323 (33) |
| Mean HCV RNA, $\log_{10}$ IU/mL (SD) | 6.3 (0.70) | 6.3 (0.70) |

BMI, body mass index; IL28B, interleukin-28B.

- Patients on OST were younger and included a greater proportion of men than those not on OST

### HCV Genotype

| GT, n (%) | OST n=51 | Non-OST n=984 |
|---|---|---|
| 1 | 13 (25) | 315 (32) |
| 1a | 12 (24) | 198 (20) |
| 1b | 1 (2) | 117 (12) |
| 2 | 8 (16) | 230 (23) |
| 3 | 24 (47) | 253 (26) |
| 4 | 6 (12) | 110 (11) |
| 5 | 0 | 35 (4) |
| 6 | 0 | 41 (4) |

GT, genotype.

- HCV genotype 3 predominated in patients on OST

## Results (cont'd)

### Concomitant OST Medication

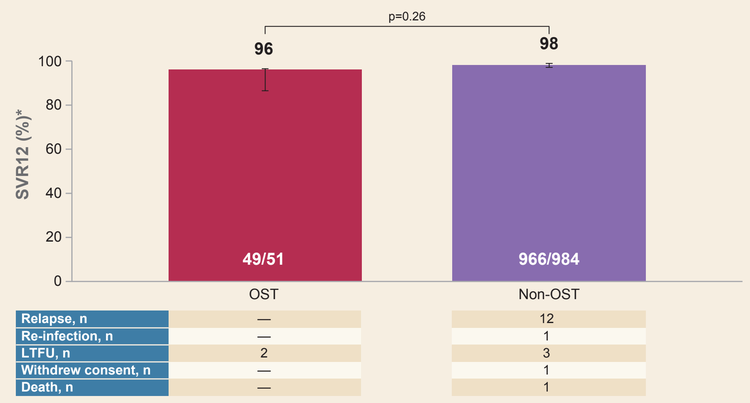
| Medication, n (%) | OST n=51 |
|---|---|
| Methadone | 34 (67) |
| Buprenorphine | 17 (33) |

### Disposition

| Patients, n (%) | OST n=51 | Non-OST n=984 |
|---|---|---|
| Completed treatment | 49 (96) | 981 (>99) |
| Discontinuations | 2 (4) | 3 (<1) |
| AE | 1 (2) | 1 (<1) |
| Lack of efficacy | 0 | 1 (<1) |
| Nonadherence | 0 | 0 |
| Lost to follow-up | 1 (2) | 1 (<1) |

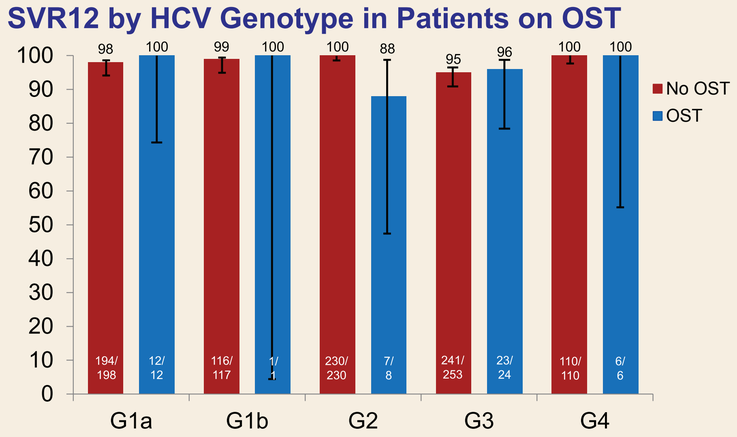
- 1 patient on OST discontinued treatment after 1 dose of study drug due to AEs of anxiety, headache, and disturbance in attention

### SVR12




*Error bars represent 95% confidence intervals (CIs). LTFU, lost to follow-up.

### SVR12 by HCV Genotype in Patients on OST




*Error bars represent 95% CIs.

### Safety

| | Patients, n (%) | OST n=51 | Non-OST n=984 |
|---|---|---|---|
| Adverse Events | AE | 44 (86) | 778 (79) |
| | Grade 34 AE | 7 (14) | 26 (3) |
| | Serious AE | 3 (6) | 20 (2) |
| | Discontinuation due to AE | 1 (2) | 1 (<1) |
| | Death | 0 | 3 (<1) |
| Laboratory Abnormalities | Grade 3–4 | 4 (8) | 73 (7) |
| | Hb <10 g/dL | 0 | 2 (<1) |
| | Hb <8.5 g/dL | 0 | 0 |

- The proportion with AEs (86% vs 79%, p=0.29) were similar among participants receiving and not receiving OST. The proportion with serious AEs (6% vs. 2%, p=0.10) were higher in those receiving OST, but not statistically significant
- Serious adverse events in those receiving OST included abdominal pain (n=1), bronchitis (n=1), and palpitations (n=1)

### Adverse Events in ≥10% of Patients

| AE, n (%) | OST n=51 | Non-OST n=984 |
|---|---|---|
| Headache | 11 (22) | 285 (29) |
| Fatigue | 10 (20) | 207 (21) |
| Nausea | 11 (22) | 124 (13) |
| Nasopharyngitis | 5 (10) | 116 (12) |

- The most common AEs were similar between the 2 treatment groups

### Adherence

| | OST n=51 | Non-OST n=984 | p-Value |
|---|---|---|---|
| Mean adherence, % (range) | 93 (0–100) | 98 (14–100) | |
| Adherence rate ≥90%, n (%) | 46 (90)* | 946 (96) | 0.06 |

*5 patients had adherence <90%: 3 patients did not return study drug bottles and adherence could not be determined, 1 patient discontinued due to AE, and 1 patient was LTFU.

- Study drug adherence was similar between the 2 treatment groups

## Conclusions

- The pangenotypic SOF/VEL fixed-dose combination provided a highly effective treatment for HCV patients on OST
- SOF/VEL was well tolerated, with a similar AE profile for patients on OST compared with those not on OST
- There were no cases of HCV reinfection in the 24 weeks following the end of treatment among participants receiving OST. One patient not receiving OST that was determined to have HCV re-infection by deep sequencing at time of virologic failure (pre-treatment genotype 3; reinfection genotype 1a).
- Further prospective evaluation of SOF/VEL in patients who inject drugs is ongoing

## References & Acknowledgments


1. Curry MP, et al. N Engl J Med 2015;373:2618-28
2. Feld JJ, et al. N Engl J Med 2015;373:2599-607
3. Foster GR, et al. N Engl J Med 2015;373:2608-17



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