Efficacy of Sofosbuvir/Ledipasvir With and Without Ribavirin in Patients with Chronic HCV Genotype 1 Infection Receiving Opioid Substitution Therapy: Analysis of Phase 3 ION Trials

Poster Number 27

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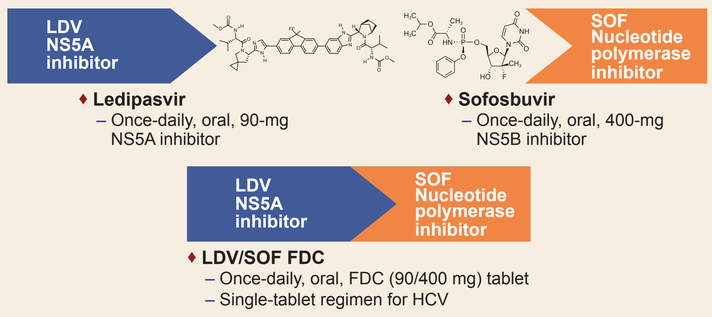
Introduction



FDC, fixed-dose combination; HCV, hepatitis C virus.

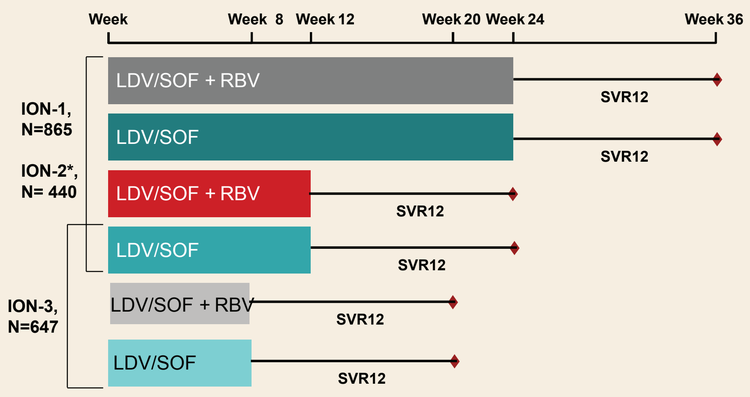
- People with a history of injecting drug use include former injectors who have ceased injecting and "recent PWID" (definitions for "recent" vary from one month to 12 months)[1]
- People with a history of injecting drug use may also be receiving opioid substitution therapy (OST, methadone or buprenorphine) for management of opioid dependence, some of whom may also have recently injected drugs

Objectives

- To perform a post-hoc analysis of the Phase 3 ION trials to evaluate the impact of OST and illicit drug use during therapy on treatment completion, adherence, efficacy and safety of LDV/SOF +/- RBV

Methods

ION Phase 3 Study Designs



RBV, ribavirin

- A post-hoc analysis was performed using data from ION-1, -2 and -3 (ClinicalTrials.gov NCT01701401(2), NCT01768286(3), NCT01851330(4) respectively).
- Patients with HCV genotype (GT) 1, treatment naive, with /without compensated cirrhosis received 8, 12, or 24 weeks of LDV/SOF +/- RBV
- Participants receiving OST (e.g. methadone or buprenorphine) were eligible for inclusion. Patients with positive urine drug test (cannabinoids not tested) at screening that was not explained by a prescribed medication were excluded from enrollment
- Stored serum samples from ION-1 retrospectively tested at Week 8 and 12 for illicit drugs (amphetamines, methamphetamines, barbiturates, benzodiazepines, cocaine, methadone, opiates, oxycodone, phencyclidine, propoxyphene and cannabinoids) by enzyme-linked immunosorbent assay
- Treatment completion, adherence, SVR12, safety and reinfection were assessed
- 853 of 865 patients treated in the ION-1 study had Week 8 or Week 12 serum sample available for retrospective testing of drugs
- Phylogenetic analyses were used to distinguish viral relapse from reinfection

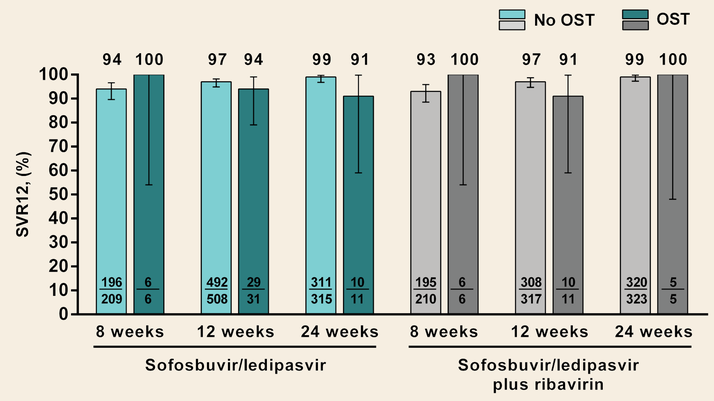
Results

Demographics by receipt of OST- ION Phase 3 studies

Characteristic	OST at enrollment (n = 70)	No OST at enrollment (n = 1882)
Mean (SD) age, years	47 (11)	53 (10)
Male sex, n (%)	48 (69)	1127 (60)
Race, n (%)		
White	63 (90)	1537 (82)
Black	6 (9)	302 (16)
Mean (SD) BMI	28 (6)	27 (5)
OST, n (%)		
Methadone	40 (57)"	N/A
Buprenorphine	29 (41)	N/A
Naloxone*	2 (3)	N/A
HCV GT1a, n (%)	63 (90)	1380 (73)
IL28B CC, n (%)	28 (40)	455 (24)
Mean (SD) HCV RNA $\log_{10}$ IU/mL	6.4 (0.8)	6.4 (0.7)
Cirrhosis, n (%)	7 (10)	217 (12)
Treatment-experienced n (%)	8 (11)	432 (23)

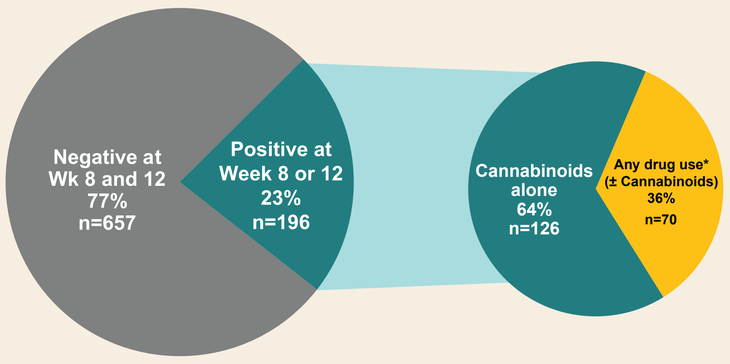
Abbreviations: BMI, body mass index; HCV, hepatitis C virus; OST, opioid substitution therapy; SD, standard deviation; ULN, upper limit of normal. *One patient was receiving naloxone plus methadone; one patient was taking naloxone following back surgery.

SVR 12 by receipt of OST- ION Phase 3 studies



Error bars represent 95% CI

Positive Drug Test Without Prescription = On-Treatment Illicit Drug Use (ION-1)



*Includes non-prescribed benzodiazepines (n=19, 27%),opiates/oxycodone/methadone (n=11, 16%), cocaine (n=9, 13%), methamphetamine/amphetamine (n=7, 10%), and barbiturates (n=7, 10%).

Baseline Demographics stratified by Illicit Drug Use- ION -1

Characteristic, n (%)	No Illicit Drugs n=657	Cannabinoids Only n=126	Any Illicit Drugs ± Cannabinoids n=70
Mean (SD) age, years	53 (11)	51 (11)	51 (10)
Male sex	376 (57)	90 (71)	40 (57)
White race	553 (84)	109 (87)	64 (91)
OST	20 (3)	3 (2)	12 (17)
IFNL3 CC genotype	178 (27)	44 (35)	29 (41)
HCV genotype 1a	415 (63)	102 (81)	54 (77)
No cirrhosis	550 (84)	107 (85)	58 (83)

Abbreviations: HCV, hepatitis C virus; SD, standard deviation.

Disposition - By OST Therapy At Baseline (Phase 3 ION studies)

Characteristic	Treatment completion n (%)	≥80 adherence n (%)	SVR12 n (%)	Adverse events n (%)	Serious adverse events n (%)
Opioid substitution therapy					
No (n = 1,882)	1846 (98%)	1737 (92%)	1822 (97%)	1498 (80%)	49 (3%)
Yes (n = 70)	68 (97%)	65 (93%)	66 (94%)	62 (89%)	3 (4%)

Disposition- By Illicit Drug Use during Therapy (ION-1)

Characteristic	Treatment completion n (%)	≥80 adherence n (%)	SVR12 n (%)	Adverse events n (%)	Serious adverse events n (%)
Illicit drug use during therapy					
None (n = 657)	643 (98%)	598 (91%)	652 (99%)	564 (86%)	27 (4%)
Cannabinoids only (n = 126)	124 (98%)	116 (92%)	123 (98%)	104 (83%)	2 (2%)
Illicit drugs ± cannabinoids (n = 70)	68 (97%)	64 (91%)	68 (97%)	63 (90%)	3 (4%)

Adverse Events

Adverse event, n (%)	OST at enrollment: LDV/SOF (n = 48)	OST at enrollment: LDV/SOF + RBV (n = 22)	No OST at enrollment: LDV/SOF (n = 1032)	No OST at enrollment: LDV/SOF + RBV (n = 850)
Any	43 (90)	19 (86)	766 (74)	732 (86)
Serious	2 (4)	1 (5)	32 (3)	17 (2)
Most common (>10% in any treatment group)				
Fatigue	15 (31)	8 (36)	227 (22)	325 (38)
Headache	12 (25)	4 (18)	212 (21)	227 (27)
Nausea	9 (19)	8 (36)	103 (10)	145 (17)
Insomnia	5 (10)	4 (18)	78 (8)	150 (18)
Irritability	3 (6)	4 (18)	44 (4)	91 (11)
Asthenia	1 (2)	4 (18)	37 (4)	52 (6)
Decreased appetite	5 (10)	1 (5)	23 (2)	34 (4)
Back pain	4 (8)	3 (14)	40 (4)	38 (5)
Rash	3 (6)	3 (14)	45 (4)	91 (11)
Cough	3 (6)	1 (5)	39 (4)	90 (11)
Hypertension	2 (4)	3 (14)	24 (2)	19 (2)
Hemoglobin level <10 g/dL	0	1 (5)	1 (<0.1)	57 (7)

Conclusions

- The ION clinical trials demonstrates that there is no difference in treatment completion, adherence, SVR12 and AEs among people receiving and not receiving OST who received treatment with ledipasvir/sofosbuvir ± ribavirin
- Further, among people without drug use at the time of therapy initiation, subsequent illicit drug use during therapy did not have a major impact on treatment completion, adherence, SVR12 and AEs
- There were no cases of HCV reinfection observed in this study through 24 weeks after treatment completion
- These data demonstrate that ledipasvir/sofosbuvir HCV therapy is well tolerated and effective among PWID receiving OST and those with illicit drug use during HCV therapy
- Clinical trials are evaluating interferon-free therapy among PWID with recent drug use and PWID with recent drug use and/or those receiving OST are ongoing

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Acknowledgments

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