The single tablet regimen of ledipasvir/sofosbuvir is efficacious and well-tolerated among people receiving opioid substitution therapy

Reau N[1], Grebely J[2], Mauss S[3], Brown A[4], Puoti M[5], Wyles D[6], Natha M[7], Yun C[7], Zhu Y[7], Kreter B[7], Brainard DM[7], Carr V[7], Dore GJ[2]

[1]Rush University Medical Center, Chicago, USA [2]The Kirby Institute, UNSW Australia, Sydney, NSW, Australia [3]Center for HIV and Hepatogastroenterology, Duesseldorf, Germany [4]Liver Unit, Department of Medicine, St Mary's Hospital, London, United Kingdom [5]Azienda Ospedaliera Ospedale Niguarda Ca' Granda, Milan, Italy [6]Division of Infectious Diseases University of California, San Diego, USA [7]Gilead Sciences, Foster City, USA.

Background

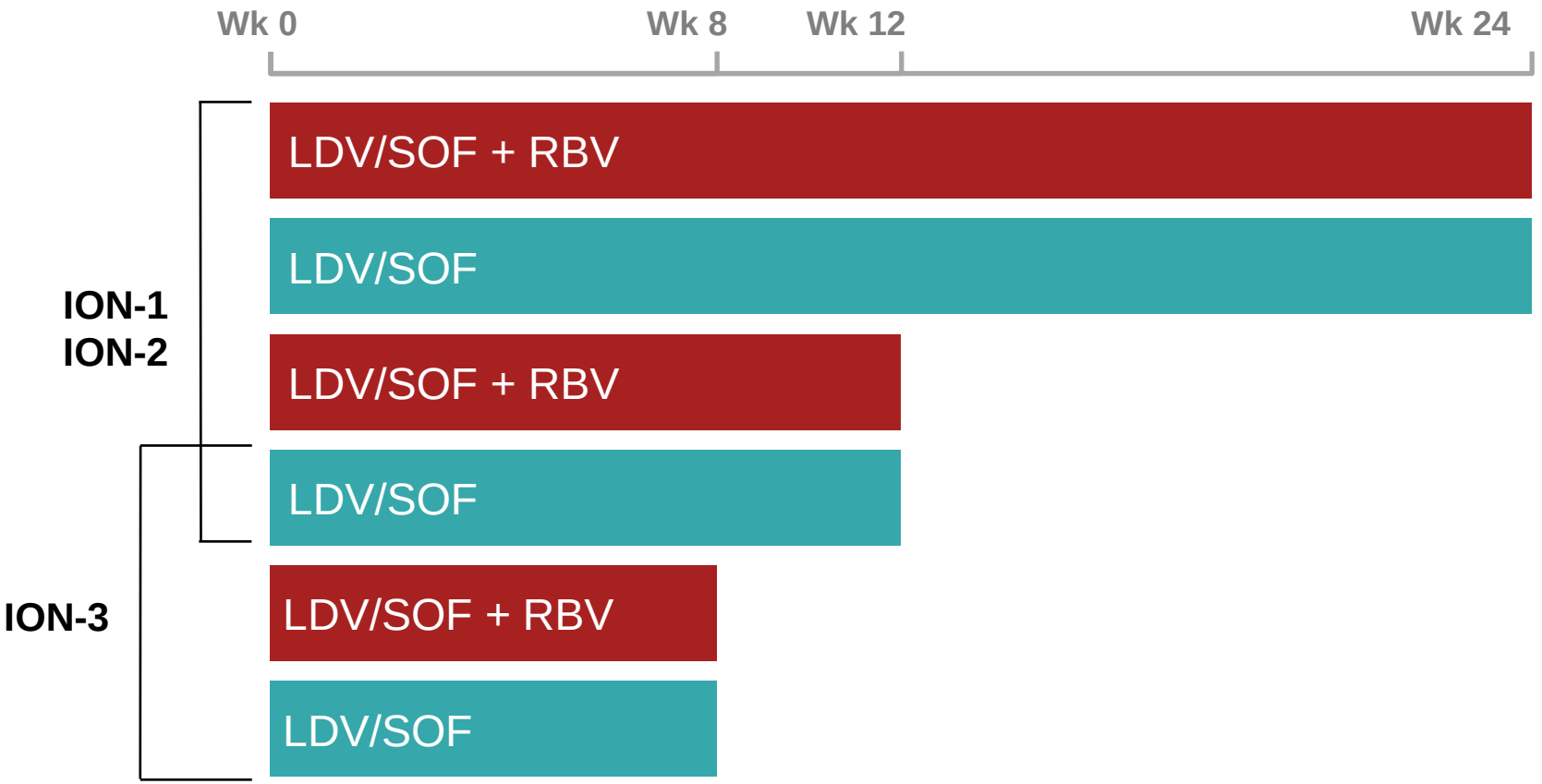
- Hepatitis C virus (HCV) infection disproportionally affects people who inject drugs (PWID) [1-2]
- Effective HCV treatment for PWID is necessary to prevent the development and progression of liver disease and stop onward transmission[1-2]
- Interferon-based HCV treatment has been shown to be effective among PWID and people receiving OST[3-4]; however, safety and efficacy of DAAs in this patient group are lacking
- Ledipasvir/Sofosbuvir (LDV/SOF) is a once daily, single tablet regimen which has shown to be well-tolerated and effective for treatment of chronic HCV genotype 1 patients with and without compensated cirrhosis[5-7]

1) Grebely J. et al. Int J Drug Policy **2015**; 26(10): 1028-38. 2) Martin NK et al. Hepatology **2013**; 58(5): 1598-609. 3) Aspinall EJ et al. Clin Infect Dis. 2013; 57 S2:S80-9; 4) Dimova RB, et al. Clin Infect Dis. 2013; 56(6):806-16. 5) Afdhal N et al. N Engl J Med 2014; 370(20):1889-98; 6) Afdhal N et al. N Engl J Med 2014; 370(16):1483-93; 7) Kowdley KV et al. N Engl J Med 2014; 370(20):1879-88.

Objective

- To compare efficacy, adherence, and tolerability of LDV/SOF ± ribavirin in participants receiving and not receiving OST in the ION Phase 3 trials

LDV/SOF Phase 3 Program (ION-1, ION-2, ION-3)[1-3]



- ION-1: GT-1 HCV treatment-naïve,16% with cirrhosis; N = 865
- ION-2: GT-1 HCV treatment-experienced, 20% with cirrhosis; N = 440
- ION-3: GT-1 HCV treatment-naïve, without cirrhosis; N = 647

Patients were excluded if deemed to have clinically relevant drug abuse within 12 months of screening.

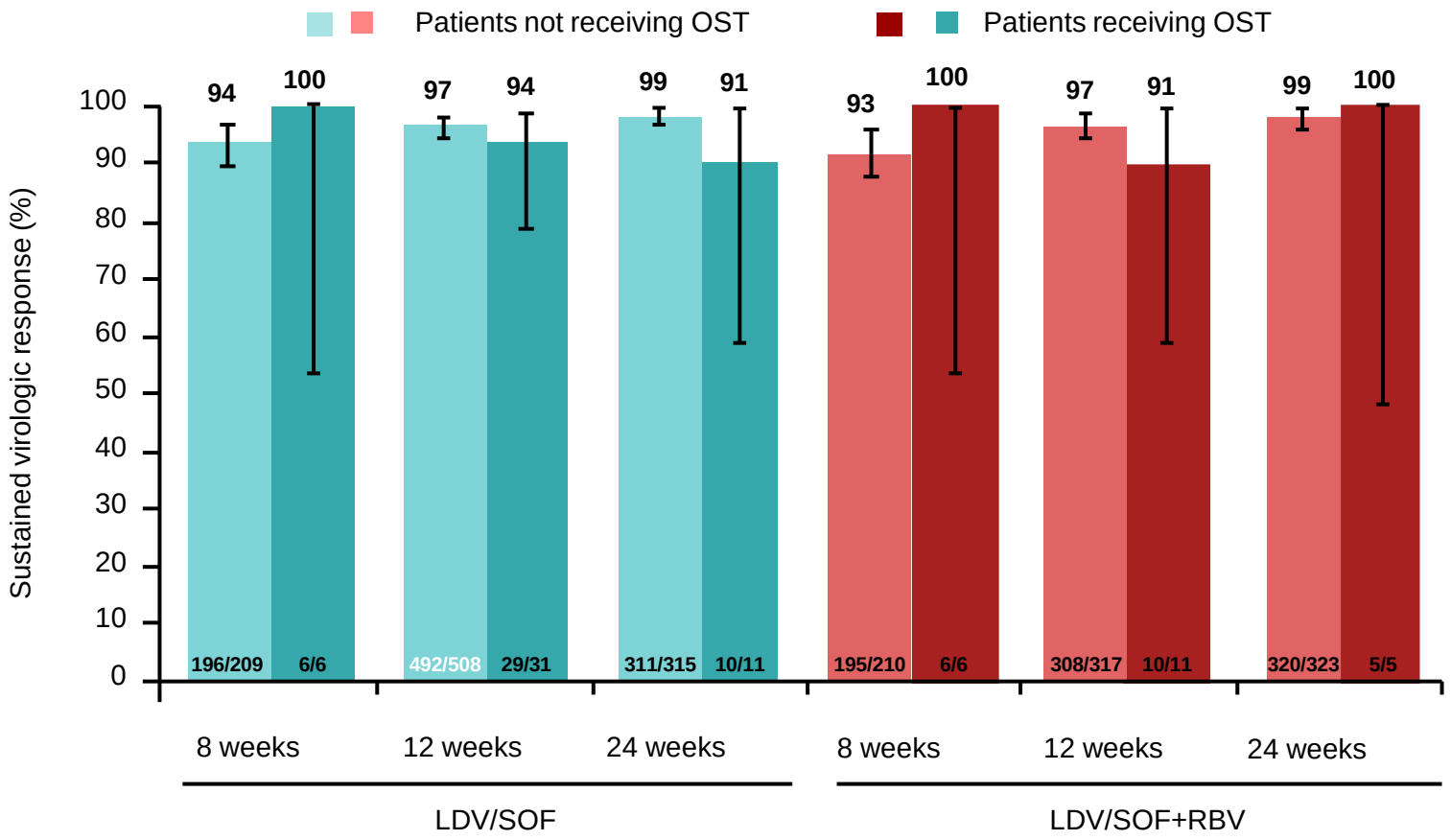
1) Afdhal N et al. N Engl J Med 2014; 370(20):1889-98; 2) Afdhal N et al. N Engl J Med 2014; 370(16):1483-93; 3) Kowdley KV et al. N Engl J Med 2014; 370(20):1879-88.

Demographics and Baseline Characteristics

	OST at enrollment n=70	No OST at enrollment n=1882
Mean (SD) age, years	47 (11)	53 (10)
Male, n (%)	48 (69)	1127 (60)
White, n (%)	63 (90)	1537 (82)
OST, n (n%)		
Methadone	40 (57)	–
Buprenorphine	30 (43)	–
Cirrhosis, n (%)		
Yes	7 (10)	217 (11.5)
No	63 (90)	1660 (88.2)
Missing	0	5 (0.3)
Prior treatment experience, n (%)		
Treatment naive	62 (89)	1450 (77)
Treatment experienced	8 (11)	432 (23)

Results: Efficacy (ITT Analysis)

Overall, 70/1,952 participants received OST in the ION Phase 3 program



No cases of HCV reinfection were observed up to SVR24

Results: Adverse events

Adverse event, n (%)	OST at enrollment		No OST at enrollment	
	LDV/SOF (n=48)	LDV/SOF + RBV (n=22)	LDV/SOF (n=1032)	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)	67 (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)

Adverse events mostly mild or moderate in severity

Results: Virologic and Safety Outcome

Outcome, n (%)	OST at enrolment (n=70) n, %	No OST at enrolment (n=1882) n, %	P Value
Treatment completion	68 (97%)	1,846 (98%)	0.40
≥80% adherence	65 (93%)	1,737 (92%)	0.042
SVR12	66 (94%)	1822 (97%)	0.29
Adverse events	62 (89%)	1498 (80%)	0.07
Serious adverse events	3 (4%)	49 (3%)	0.43

Conclusions

- The interferon-free, once-daily, single tablet regimen of LDV/SOF achieved high and comparable SVR12 among people with HCV genotype 1 regardless of OST use
- LDV/SOF was well-tolerated and reports of adverse events were similar among those receiving and not receiving OST
- There were no cases of reinfection 24 weeks after treatment completion
- These data support the use of LDV/SOF for HCV treatment for PWID receiving OST
- Further studies are needed to evaluate LDV/SOF among active PWID

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