Adherence to sofosbuvir and velpatasvir among people with chronic HCV infection and recent injection drug use: the SIMPLIFY study

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21 September, 2018

UNSW SYDNEY Kirby Institute

Disclosures

Nothing to disclose

Background/rationale

- There is a significant burden of hepatitis C virus infection among people who inject drugs globally[1]
- In order to reach the targets set by the WHO, scale up of HCV therapy among people who inject drugs is crucial
- Treatment has been shown to be safe and effective in people who inject drugs
    - 94% SVR in SIMPLIFY
- Adherence to therapy has been one of the major concerns around scale up of HCV DAA treatment among people who inject drugs

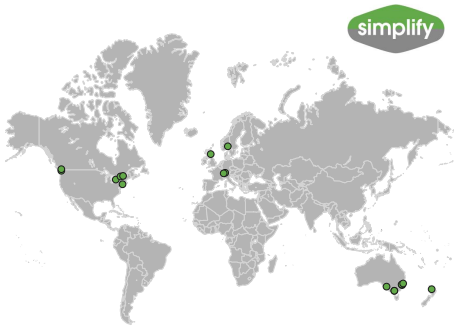
[1]Grebely et al, 2018, Addiction

Aims

1. Investigate the daily adherence to HCV DAA therapy among people with recent injection drug use
2. Assess factors associated with non-adherence to therapy
3. Investigate the change in adherence over the course of treatment

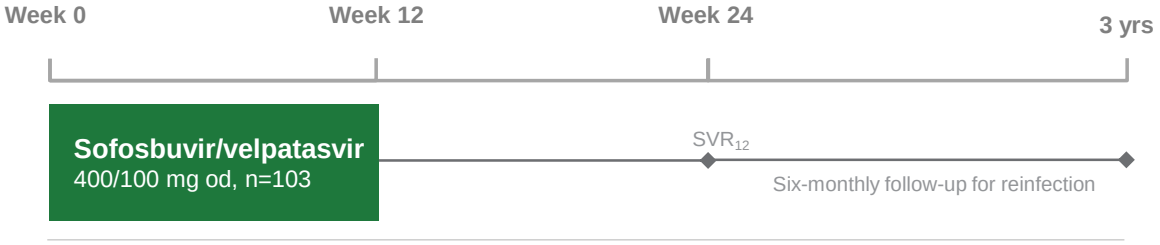
SIMPLIFY study design

- Investigator-initiated, Kirby/UNSW sponsored, international open-label trial
- 19 sites, 7 countries
- Study recruitment conducted through a network of drug and alcohol clinics (n=1), hospital clinics (n=12), and community clinics (n=2)
- Participants enrolled between April 2016 and October 2016



Study design and participant eligibility

- DAA treatment-naïve patients with GT1-6 chronic HCV infection (F0-4)
- People with recent injecting drug use (past six months)
- Participants with HIV and decompensated liver disease excluded
- Electronic blister packs to monitor adherence



Treatment adherence

- Measured using an electronic blister-pack
  - Administered weekly
- Calculated as the number of doses removed from the blister-pack (max one per day) divided by the number of expected doses (84 doses).

Study outcomes and statistical analysis

Non-adherence

- Receiving <90% of doses to a maximum of one dose per day

Inconsistent dose timing

- Standard deviation of daily dose timing of ≥240 minutes

Ongoing daily adherence

- Mean adherence for the population by treatment day

Logistic regression used to assess factors associated with study outcomes

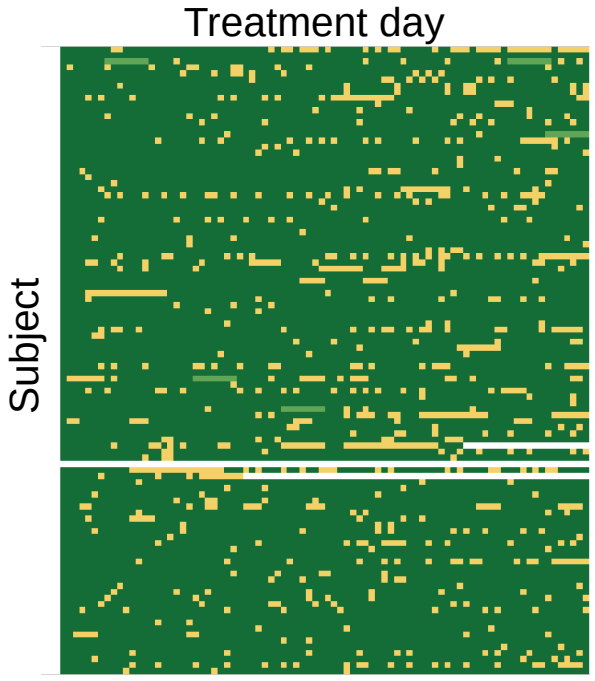
Participant characteristics

Characteristic	SOF/VEL (12 weeks) N = 103
Female, n (%)	29 (28%)
Age, median years (25%, 75%)	48 (41, 53)
Any injecting drug use (last 30 days), n (%)	76 (74%)
Heroin	57 (55%)
Methamphetamines	31 (30%)
Other opioids	22 (21%)
Cocaine	13 (13%)
≥Daily injecting drug use (last 30 days), n (%)	27 (26%)
Current opioid substitution therapy, n (%)	
Methadone	45 (44%)
Buprenorphine ± naloxone	16 (16%)

Participant characteristics

Characteristic	SOF/VEL (12 weeks) N = 103
HCV genotype, n (%)	
1	36 (35%)
2	5 (5%)
3	60 (58%)
4	2 (2%)
Fibrosis stage (METAVIR), n (%)	
F0-F1	59 (62%)
F2-F3	27 (28%)
F4	9 (9%)
Study site distribution, n (%)	
Canada/US	40 (39%)
Europe	20 (19%)
Australasia	43 (42%)

Overall adherence of 94%



Completion and adherence

	Overall (n=103)
Treatment completion	100 (97%)
Missed doses (adherence %)	
No missed doses (100%)	12 (12%)
1-8 missed doses (90%-<100%)	56 (54%)
>8 missed doses (<90%; non-adherent)	35 (34%)
Longest episode of non-adherence	
1 day	44 (43%)
2 days	19 (18%)
3 days	3 (3%)
4 days	9 (9%)
5 days	2 (2%)
6 days	3 (3%)
≥7 days	11 (11%)

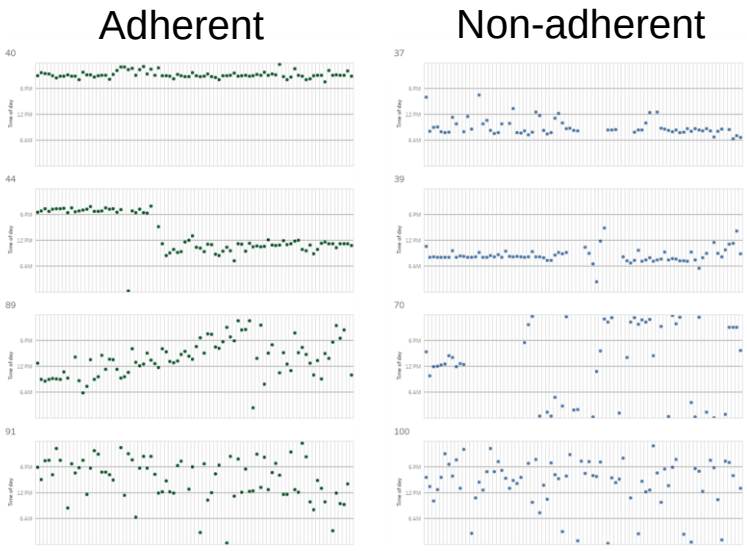
Factors associated with non-adherence

	Sofosbuvir/velpatasvir adherence of ≥90%	Sofosbuvir/velpatasvir adherence of <90%	Unadjusted OR	P
Gender				
Female	23 (79)	6 (21)	1.00	-
Male	47 (64)	27 (36)	0.45 (0.16-1.25)	0.128
Current OST				
No	32 (71)	13 (29)	1.00	-
Yes	38 (66)	20 (34)	1.30 (0.56-3.01)	0.547
Injecting (last month)				
No	20 (74)	7 (26)	1.00	-
Yes	50 (66)	26 (34)	1.49 (0.56-3.97)	0.430
Frequency of injecting (last month)				
Never	20 (74)	7 (26)	1.00	-
Less than daily	31 (63)	18 (37)	1.66 (0.59-4.69)	0.339
Daily or greater	19 (70)	8 (30)	1.20 (0.36-3.97)	0.761
Stimulant injecting (last month)				
No	47 (77)	14 (23)	1.00	-
Yes	23 (55)	19 (45)	2.77 (1.18-6.50)	0.019

Factors associated with non-adherence

	Sofosbuvir/ velpatasvir adherence of ≥90%	Sofosbuvir/ velpatasvir adherence of <90%	OR (95% CI)	P	aOR (95% CI)	P
OST while on treatment						
No	33 (80)	8 (20)	1.00	-	-	-
Yes	37 (62)	23 (38)	2.56 (1.01-6.51)	0.048	-	-
Injecting while on treatment						
No	12 (67)	6 (33)	1.00	-	-	-
Yes	58 (70)	25 (30)	0.86 (0.29-2.55)	0.789	-	-
Stimulant injecting while on treatment						
No	44 (80)	11 (20)	1.00	-	-	-
Yes	26 (57)	20 (43)	3.01 (1.27-7.14)	0.012	3.39 (1.19-9.67)	0.023
Consistency in dose timing (standard deviation in minutes)						
<240	12 (34)	23 (66)	1.00	-	-	-
≥ 240	58 (87)	9 (13)	12.35 (4.59-33.24)	<0.001	12.44 (4.37-35.41)	<0.001

Examples of adherence patterns

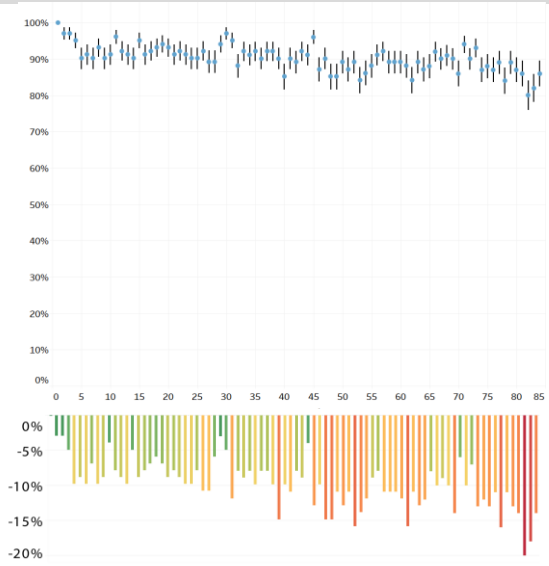


Consistency in dose timing

	Overall (n=103)
Consistency in dose timing (standard deviation in minutes)*	
<120	24 (24%)
≥ 120-<240	43 (42%)
≥ 240	35 (34%)

	Standard deviation of dose timing of <240 minutes	Standard deviation of dose timing of ≥240 minutes	OR (95% CI)	P	aOR (95% CI)	P
Education						
High school or greater	37 (76)	12 (24)	1	-	-	-
<High school	30 (57)	23 (43)	2.36 (1.01-5.52)	0.047	2.77 (1.14-6.72)	0.025
Stimulant injecting (last month)						
No	44 (72)	17 (28)	1	-	-	-
Yes	23 (56)	18 (44)	2.03 (0.88-4.66)	0.097	2.43 (1.01-5.85)	0.048

Decline in adherence over treatment course



Discussion

- Overall high adherence and treatment completion
- Imperfect adherence was common
- Stimulant injecting was a predictor of lower adherence
- Adherence decreased while on therapy
- Did not impact SVR

Acknowledgements

SIMPLIFY study participants

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