Kirby Institute

simplify

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

Evan Cunningham | 13 August, 2018

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

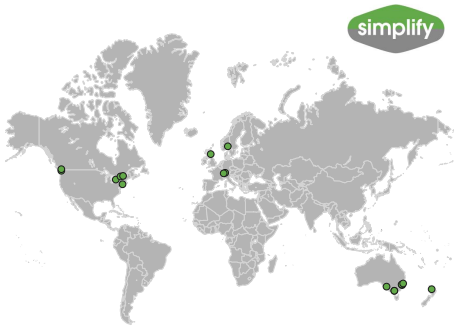
[1]Grebely et al, 2018, Addiction

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

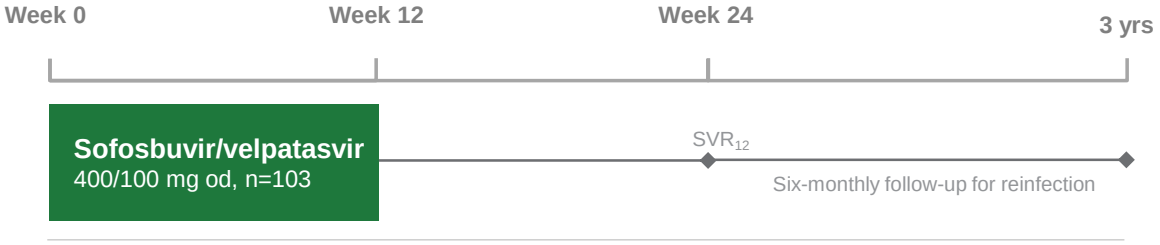
SIMPLIFY study design

- 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

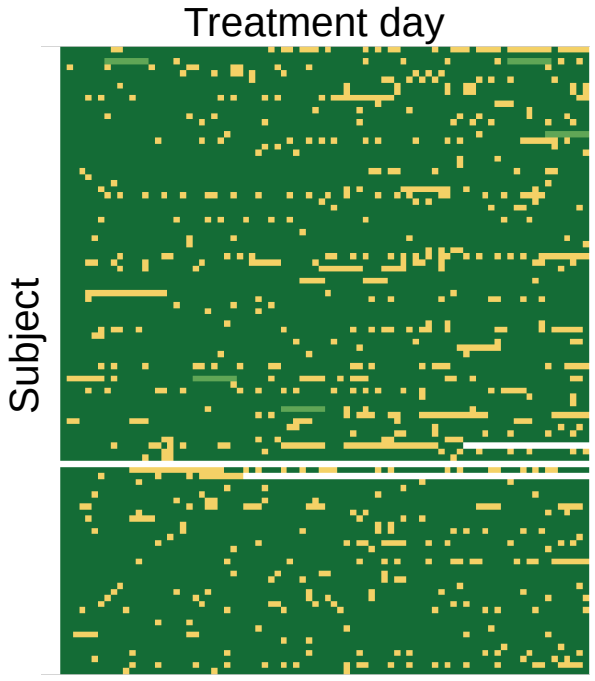
Participant characteristics

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

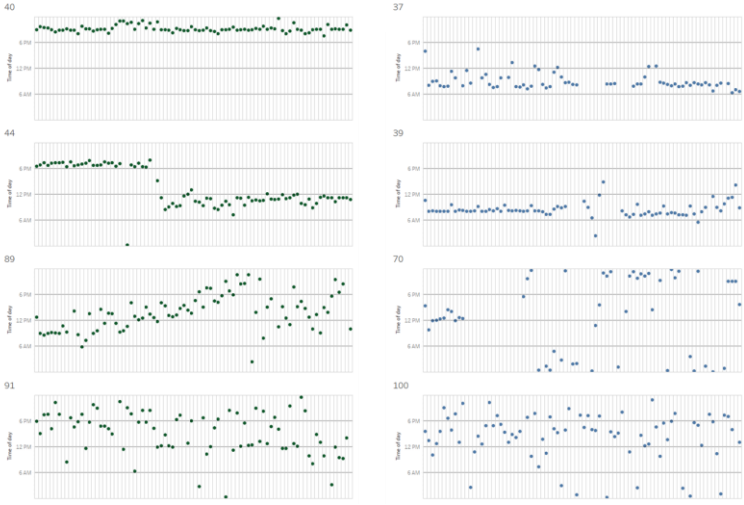
Factors associated with non-adherence

	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

Adherent

Non-adherent

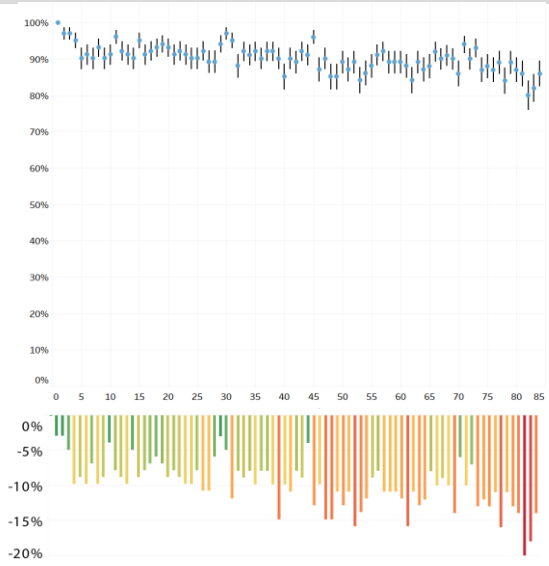


Consistency in dose timing

	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

Study coordination staff: Sophie, Amanda, Pip, Ecaterina, Mahshid

SIMPLIFY study group

Protocol Steering Committee – Gregory Dore (Chair, UNSW Sydney, Sydney, Australia), Philip Bruggmann (Arud Centres for Addiction Medicine, Zurich, Switzerland), Jason Grebely (UNSW Sydney, Sydney, Australia), Philippa Marks (UNSW Sydney, Sydney, Australia), Julie Bruneau (Centre Hospitalier de l'Université de Montréal, Canada), Tracy Swan (Médecins Sans Frontières, New York, United States), Olav Dalgard (Akershus University Hospital, Oslo, Norway), Jude Byrne (Australian Injecting & Illicit Drug Users League), Melanie Lacalamita (Poliklinik für Infektiologie, Inselspital, Bern, Switzerland) and Adrian Dunlop (Newcastle Pharmacotherapy Service, Newcastle, Australia).

Coordinating Centre – Sophie Quiene (Study Co-ordinator), Evan Cunningham (PhD Student), Behzad Hajarizadeh (Associate Lecturer), Gregory Dore (co-Principal Investigator), Jason Grebely (co-Principal Investigator), Pip Marks (Clinical Trials Manager), Ineke Shaw (Systems Manager), Sharmila Siriragavan (Data Manager) and Janaki Amin (Statistician).

Site Principal Investigators – Philip Bruggmann (Arud Centres for Addiction Medicine, Zurich, Switzerland), Julie Bruneau (Centre Hôspitalier de l'Université de Montréal, Montréal, Canada), Brian Conway (Vancouver Infectious Diseases Center, Vancouver, Canada), Olav Dalgard (Akershus University Hospital, Oslo, Norway), Gail Matthews (St Vincent's Hospital, Sydney Australia), Adrian Dunlop (Newcastle Pharmacotherapy Service, Newcastle, Australia), Margaret Hellard (The Alfred Hospital, Melbourne, Australia), Jeff Powis (South Riverdale Community Health Centre, Toronto, Canada), David Shaw (Royal Adelaide Hospital, Adelaide, Australia), Maria Christine Thurnheer (Poliklinik für Infektiologie, Inselspital, Bern, Switzerland), Martin Weltman (Nepean Hospital, Penrith, Australia), Ian Kronborg (Footscray Hospital, Footscray, Australia), Curtis Cooper (The Ottawa Hospital, Ottawa, Canada), Jordan Feld (Toronto General Hospital, Toronto, Canada), Christopher Fraser (Coolaid Community Health Centre, Victoria, Canada), Alain Litwin (Montefiore Medical Centre, New York, United States), John Dillon (Ninewells Hospital, Dundee, United Kingdom), Ed Gane (Auckland Hospital, Auckland, New Zealand), Phillip Read (Kirketon Road Centre, Sydney, Australia).

Site Co-ordinators – Jessica Andreassen, Ingunn Melkeraaen and Merete Moen Tollefsen (Akershus University Hospital, Oslo, Norway), Catherine Ferguson (Royal Adelaide Hospital, Adelaide, Australia), Nargis Abram and Vincenzo Fragomeli (Nepean Hospital, Penrith, Australia), Susan Hazelwood and Michelle Hall (Newcastle Pharmacotherapy Service, Newcastle, Australia), Tina Horschik (Arud Centres for Addiction Medicine, Zurich, Switzerland), Marie-Claire Chayer and Barbara Kotsoros (Centre Hôspitalier de l'Université de Montréal, Montréal, Canada), Melanie Lacalamita (Poliklinik für Infektiologie, Inselspital, Bern, Switzerland), Kate Mason (South Riverdale Community Health Centre, Toronto, Canada), Alison Sevehon (St Vincent's Hospital, Sydney, Australia), Hannah Pagarigan (Vancouver Infectious Diseases Center, Vancouver, Canada), Michelle Hagenauer (The Alfred Hospital, Melbourne, Australia), Rachel Liddle (Footscray Hospital, Footscray, Australia), Miriam Muir and Jessica Milloy (The Ottawa Hospital, Ottawa, Canada), Diana Kaznowski and Lily Zou (Toronto General Hospital, Toronto, Canada), Rozalyn Milne (Coolaid Community Health Centre, Victoria, Canada), Linda Agyemang and Hiral Patel (Montefiore Medical Centre, New York, United States), Shirley Clearly and Linda Johnston (Ninewells Hospital, Dundee, United Kingdom), Victoria Oliver (Auckland Hospital, Auckland, New Zealand), Rebecca Lothian and Rosemary Gilliver (Kirketon Road Centre, Sydney, Australia).