Real-world outcomes of direct-acting antiviral therapy for chronic hepatitis C following unrestricted access in Australia: The South Australian experience

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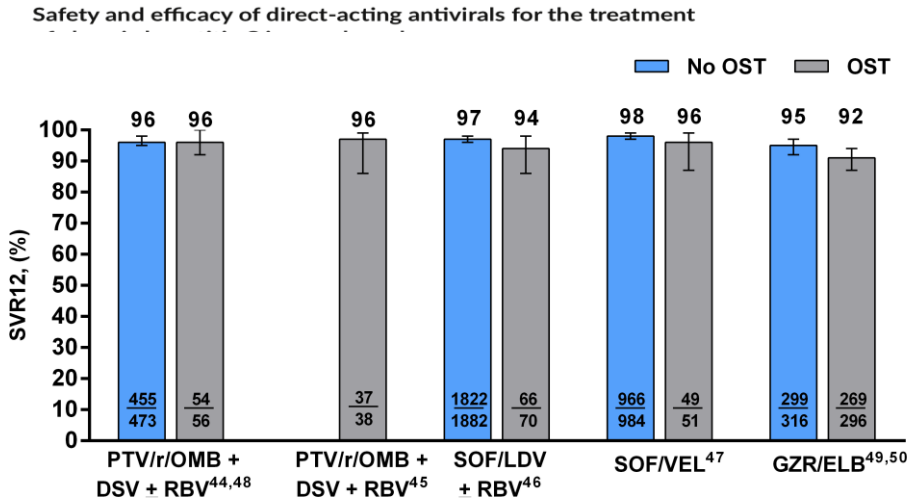
Not another real-world study?!



Australia is unique

- Any prescriber
- (Almost) any DAA regimen
- Any patient
- Unrestricted

- Most real-world outcomes examine single genotype, regimen or patient group.

What is the ‘real-world’?

- We know that DAA therapy is *efficacious*
  - There are now >200 ‘real-world’ studies
- We aimed to investigate the *effectiveness* of DAA therapy in the real-world setting where:
  - Any practitioner can prescribe (almost) any regimen to any patient.
  - Include all patients intended to start DAA treatment.

South Australia

Methods

- All patients initiated on DAA therapy at or in consultation with four South Australian tertiary centres in first 12-months of availability on PBS.
- Prospective outcome data collected at each site, supplemented with retrospective clinical data.
- Follow-up for a minimum of six-months post completion of treatment (SVR12 + 3 months, median 11 months)

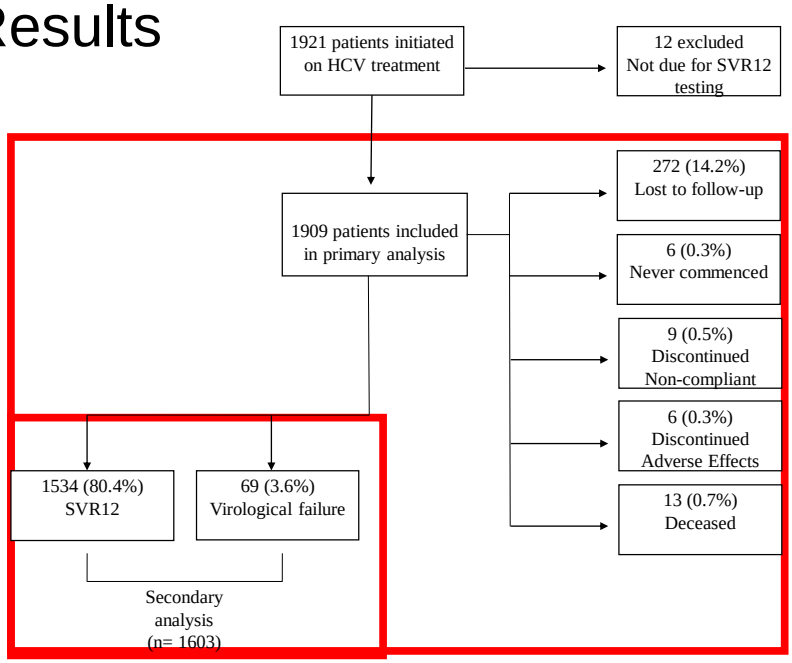
Baseline Characteristics n = 1909

Demographics	Overall	
Age (years)	54.0	(46-59)
Sex, male	1277	66.9%
Prisoner	87	4.6%
ATSI	37	1.9%
PWID, current	62	3.2%
PWID, ex	839	43.9%
PWID, never	180	9.4%
PWID, unknown	828	43.4%
Patient Residence Location		
Major City	1423	74.5%
Inner Regional	176	9.2%
Outer Regional	213	11.2%
Remote	74	3.9%
Very Remote	14	0.7%
Rural (Overall)	477	25.0%
Treatment Location		
Hospital	1456	80.3%
Remote Consultation (Community)	357	19.7%

Baseline Clinical Characteristics

Clinical Characteristics		
Diabetes	197	10.3%
HBV	13	0.7%
HIV	27	1.4%
Post-Transplant	34	1.8%
Treatment Experienced	304	18.6%
Cirrhosis, Overall	486	25.5%
Cirrhosis, Child-Pugh A	331	17.3%
Cirrhosis, Child-Pugh B	58	3.0%
Cirrhosis, Child-Pugh C	13	0.7%
Genotype 1	1088	57.0%
Genotype 2	66	3.5%
Genotype 3	729	38.2%
Genotype 4	19	1.0%
Genotype 6	6	0.3%

Results



SVR12 rates in SA

- Including all patients intended for DAA therapy:
  - Hospital-based 82%
  - Nurse-led community treatment 76%
  - Current PWID 73%
  - Remote consultation 72%
  - Prison 71%
  - ATSI 67%

Failure to check SVR12 / Loss to follow-up

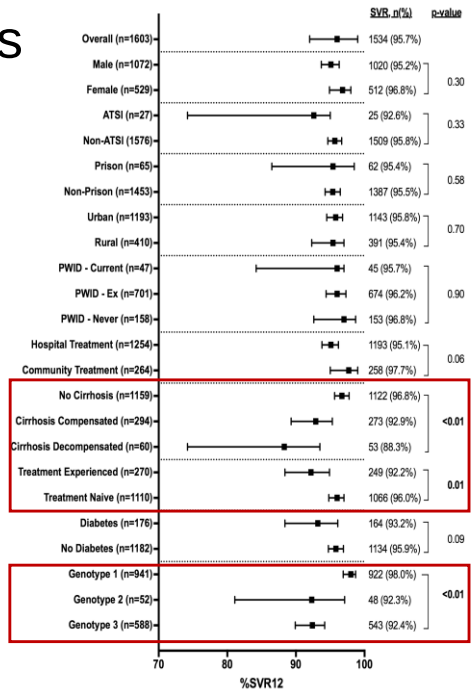
	Univariate	Multivariate analysis	
	p-value	Odds Ratio (95%CI)	p-value
Age	<0.01	0.98 (0.97 – 0.99)	0.05
Gender (Male)	0.81		
PWID	0.11		
Remote Consultation	<0.01	1.50 (1.04 – 2.18)	0.03
Prison	<0.01	2.02 (1.08 – 3.79)	0.03
Rural patient residence	0.94		
ATSI	0.20		
Cirrhosis	<0.01	0.74 (0.48 – 1.13)	0.17
Prior treatment experience	<0.01	0.79 (0.50 – 1.25)	0.31
HIV*	0.03		
HBV	0.14		
Diabetes	0.09	0.77 (0.45 – 1.33)	0.35

Prison and Remote Consultation treatments remained significant predictors of loss to follow-up (failure to test SVR12) on multivariate analysis

Secondary Analysis

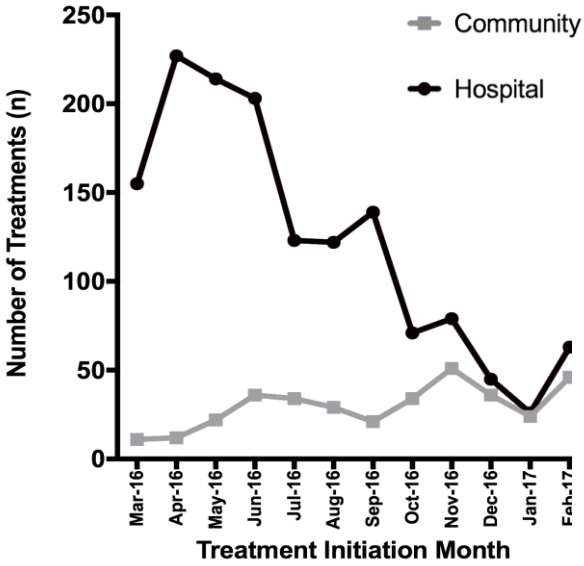
- Including only those who completed treatment and follow-up (akin to per-protocol)
- Excellent!
  - SVR12 95.7%

Lower SVR12 in cirrhosis, prior treatment experience and genotype 2/3 consistent with large trial data



Treatment initiation in SA

Significant decrease over initial twelve months



Adverse effects

- 6/1909 (0.3%) stopped treatment due to an adverse effect
  - 2 of these due to ribavirin-associated adverse effect
  - Nausea, fatigue and dizziness reported as reasons for discontinuation in others.
- 13/1909 (0.7%) mortality during treatment or SVR12 follow-up period
  - Most (7/13) were Child-Pugh B/C (sepsis listed as cause in majority).
  - Drug overdose the most common cause of mortality in non-cirrhotic deaths

We don’t always get it right

- 62/1909 patients (3.2%) were treated outside recommended guidelines
  - Most (38/62) were genotype 3
  - No difference between treatment setting (hospital or community)
  - No difference in outcome between those treated outside guidelines
  - Two virological failures in this group – both GT3, Cirrhotic, given 12-weeks Sof/Dac

People who inject drugs

- Number of current injecting drug users possibly below elimination modeling targets
  - Poor data quality surrounding PWID
  - Target 40 per 1,000 current PWID[1]
  - PWID data available for 1081/1909
    - 62 treated out of estimated 6700[2] in SA 1/3/16-28/2/17

Post treatment liver function

- Post treatment ALT above ULN in 8% of SVR12 and 39% of those with virological failure.

Limitations

- Real-world data is hampered by real-world limitations
- Missing data can be an issue. In this cohort:
  - PWID and Child-Pugh status
- Unable to gather a number of potentially important confounders:
  - Homelessness, alcohol-use disorder, mental health comorbidity
- This represents a single moment in time
  - Late SVR12 results?

Conclusions

- Outcomes are generally excellent in the Australian real-world
- Failure to test SVR12 is higher than most other published studies and significantly higher in community and prison treatments

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Questions?

References

1. Martin NK, Vickerman P, Grebely J, Hellard M, Hutchinson SJ, Lima VD, et al. Hepatitis C virus treatment for prevention among people who inject drugs: Modeling treatment scale-up in the age of direct-acting antivirals. Hepatology [Internet]. 2013 Nov;58(5):1598–609. Available from: http://doi.wiley.com/10.1002/hep.26431
2. 1. Larney S, Hickman M, Guy RJ, Grebely J, Dore G, Gray R, et al. Estimates of people who inject drugs in NSW and Australia. 2014 Sep pp. 1–17.