



HCV DAA Imports Failing to Deliver Results:

SVR12 outcomes for
imported DAA's in the NT

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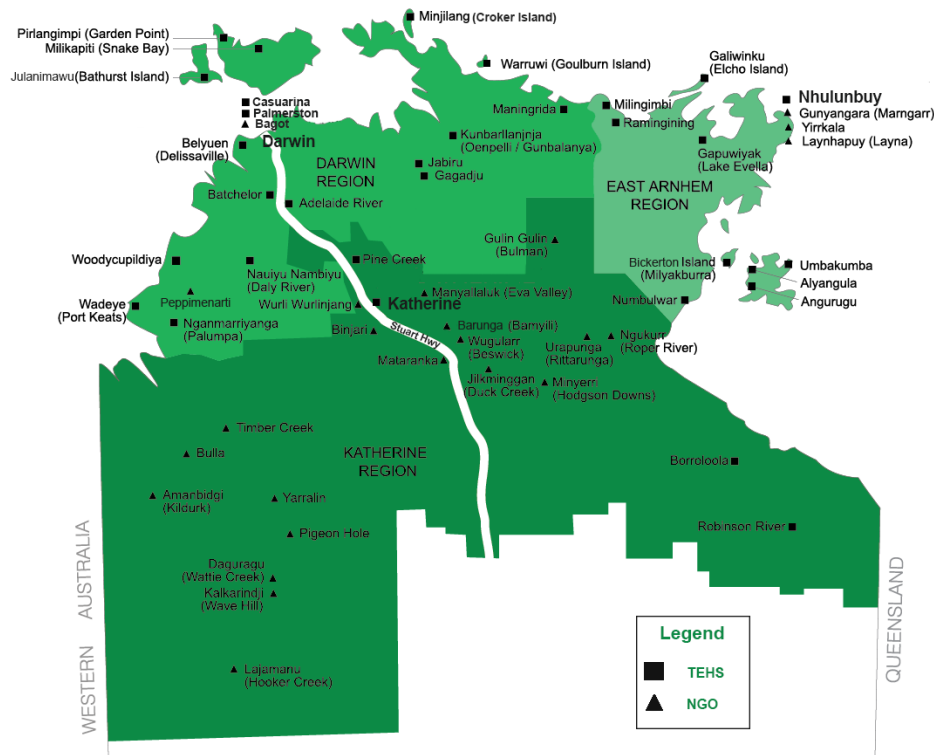
+ Declaration

- Travel support to attend educational meetings received from:
 - Abbvie, BMS, ASHM, NT Government

No ownership of share or financial interest in any pharmaceutical companies

Grant recipient from Hepatitis Australia for the B Side Project

+ HCV in the NT



The NT has two health jurisdictions

- Top End Health Service (TEHS)
- Central Australian Health Service (CAHS)

***Estimated HCV population of 3690**

Chronic HCV within the TEHS has been historically managed by the Royal Darwin Hospital Viral Hepatitis Service (RDH VHS).

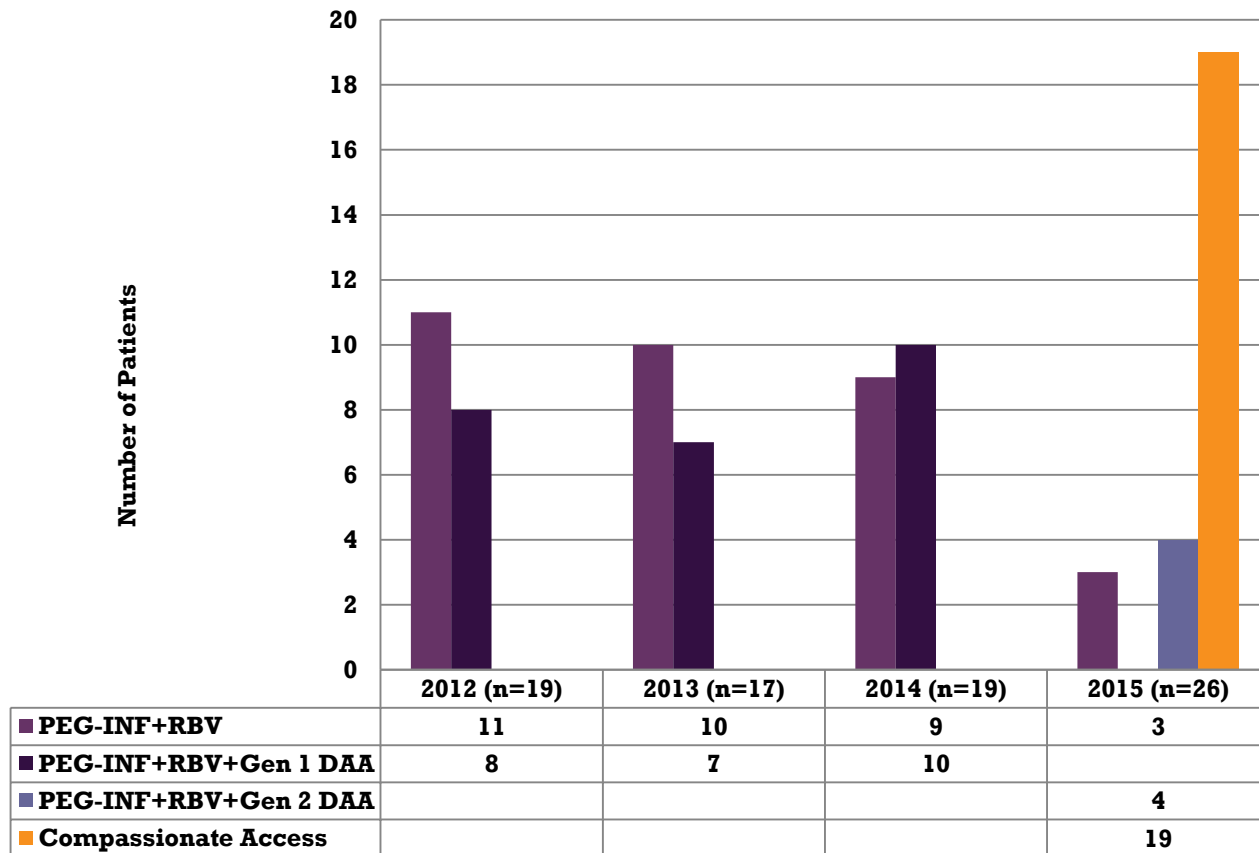
*The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual surveillance report 2015. The Kirby Institute, UNSW Australia, Sydney NSW 2052.

+ NT Treatment uptake

Historically the number of people receiving HCV treatment has been low due to:

- **Geography**
- **Unable to access clinical trials**
- **Limited access to compassionate access**
- **Contra indication to interferon based Rx**
- **Treatment toxicity**
- **Clinical resources**

+ Top End HCV Treatment 2012 - 2015



+ Awaiting PBS listing of DAA's



- The delay and uncertainty surrounding PBS listing of the DAA's lead to some individuals importing generic DAA's from overseas.
- Increased media coverage relating to importation of DAA's.
- RDH VHS agreed to support patients importing therapy after counselling around the risks involved.
- Most patients chose to await PBS listing.

+ What to do?



Motivated

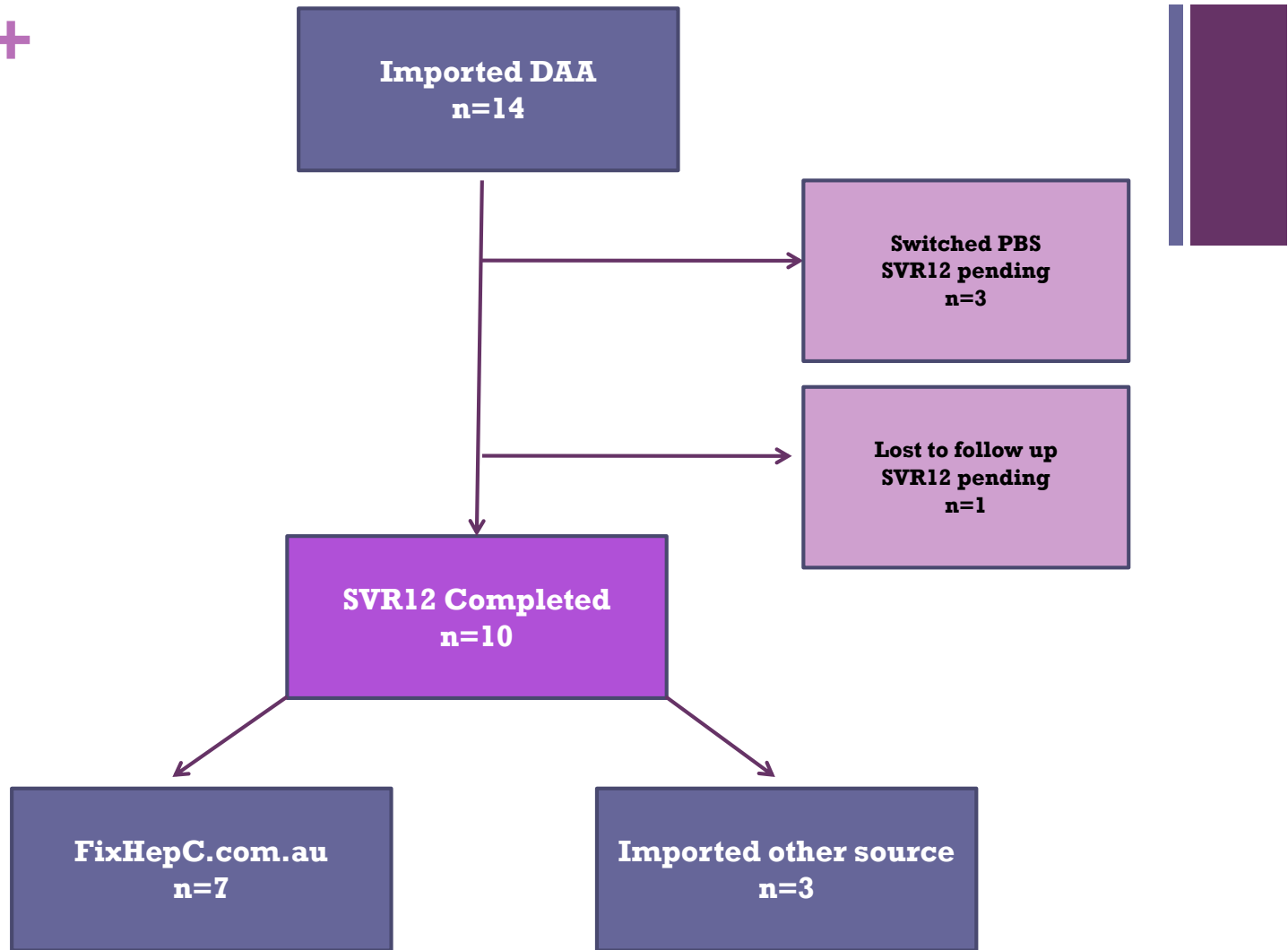
- Highly motivated to commence HCV treatment?
- Has the financial means to purchase DAA's?

Script

- Private script provided.
- Patient engaged in private arrangement to import DAA's for private use, e.g. **fixhepc.com.au**

Import

- Authenticity tested by University of Tasmania prior to individuals receiving supply.
- DAA's delivered via Australia Post to patient.
- Patients asked to contact RDH VHS and ongoing support, monitoring and follow up provided.





Patient Characteristics	n=10
Mean Age	51.7
Gender	
Male	7 (70%)
Female	3 (30%)
Cirrhosis	
Cirrhotic	2 (20%)
Non-Cirrhotic	8 (80%)
Experience	
Prior Rx	2 (20%)
Naïve	8 (80%)
Genotypes	
G1	4 (40%)
G2	1 (10 %)
G3	5 (50 %)
Imported via	
FixHepC	7 (70%)
Other source	3 (30%)

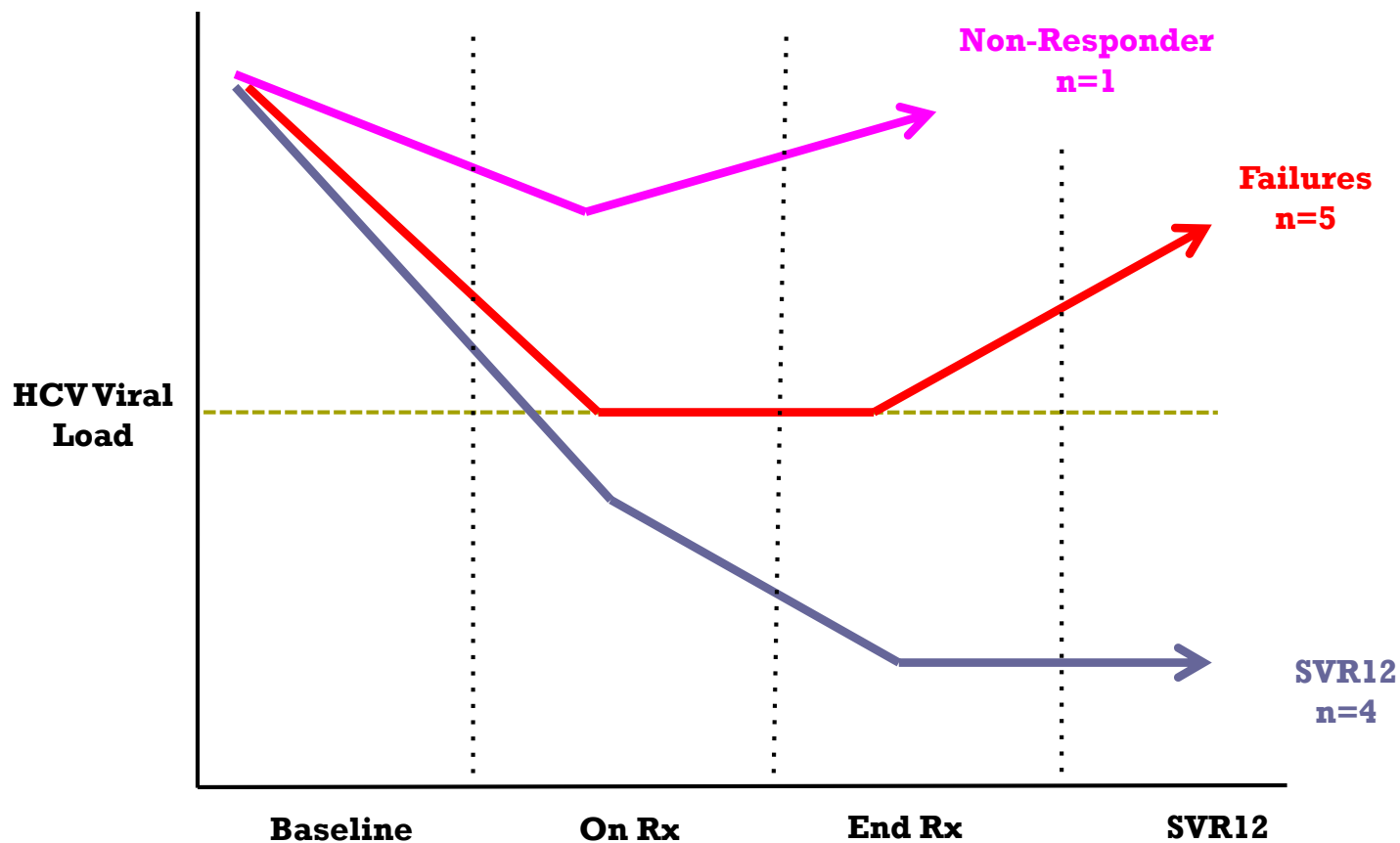


+ Treatment Regimens



Genotype	Treatment Regimes	n = 10	Cirrhotic	Rx Experienced
1	SOF + LED	4 (40%)	1	0
2	SOF + RBV	1 (10%)	0	0
3	SOF + DCV	5 (50%)	1	2

Virological response on treatment



Genotype 1- Patient Results

Non-cirrhotic - Naïve - Rx SOF+LED - Duration 12 weeks								
	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result	
	- M 37	Unk	100%	N	2,097,667 iu/ml	<12 ND	<12 Detected	Detected- PCR
	- M 58	Unk	100%	N	595,927 iu/ml	<12 ND	Not done	Achieved <12 ND
- F 26 (Not FixHepC)	N	100%	N	2,500,000 iu/ml	Not done	<12 ND	Achieved <12 ND	
Cirrhotic - Naïve - Rx SOF+LED - Duration 12 weeks								
	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	*SVR 2 Result	
	- M 59	min	100%	N	14276447 iu/ml	Not done	Not done *ALT normal	Detected 1295387iu/ml *ALT abnormal

Genotype 2- Patient Results

Non-cirrhotic - Naïve - Rx SOF+RBV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
	- M 70 Y	100%	N	34481 iu/ml	<12 detected	<12 ND	Achieved <12 ND

Genotype 3- Patient Results

Non-cirrhotic - Naïve - Rx SOF+DCV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
- F 51	N	100%	N	4,333,069	18 iu/ml	<12ND	Detected
- M 58	Y	Mostly	N	7,479,188	<12ND	<12ND	Achieved <12 ND
Non-cirrhotic - Experience - Rx SOF+DCV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
-M 50 (Not FixHepC)	N	100%	N	770,000 iu/ml	<12 Detected	<12ND	Detected
-M 53	N	100%	N	16,550,529 iu/ml	14389 iu/ml	8133365 iu/ml	Detected
Cirrhotic - Naïve - Rx SOF+DCV - Duration 24 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
-F 55 (Not FixHepC)	N	100%	Y	1603201 iu/ml	74 iu/ml	Interstate	Detected



Treatment failures



- No single factor identified resulting in treatment failure
- Self reported alcohol use was minimal
- Minimal adverse effects to treatment were reported
- 4 failures obtained through FixHepC
 - All were from different batches
- 2 failures obtained through other source
- Viral resistance testing has been arranged

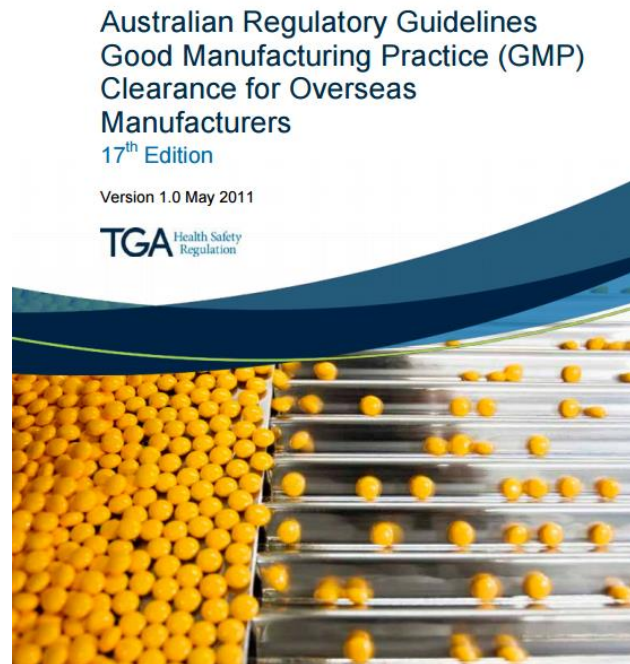
+ Viral resistance testing

- M 59: Gt 1a
 - Childs A, Rx naïve
 - 12 weeks SOF/LED
 - NS5A Y93N
- M 53: Gt 3a
 - Non cirrhotic, Rx Experienced
 - 12 weeks SOF/DCV
 - A30E & Y93H
- Y93N in GT 1 and Y93H in GT 3 have been associated with reduced efficacy of NS5A inhibitors
- The significance of A30E is unclear but A30K is associated with reduced efficacy to NS5A inhibitors

+ Factors affecting SVR12



- GMP
 - Batch quality
 - Adequate level of active agent



+ Factors affecting SVR12



- Cold Chain
- Temperature control in the tropics
- DAA delivered in wet season
 - High humidity
 - Average Temp 33 degrees

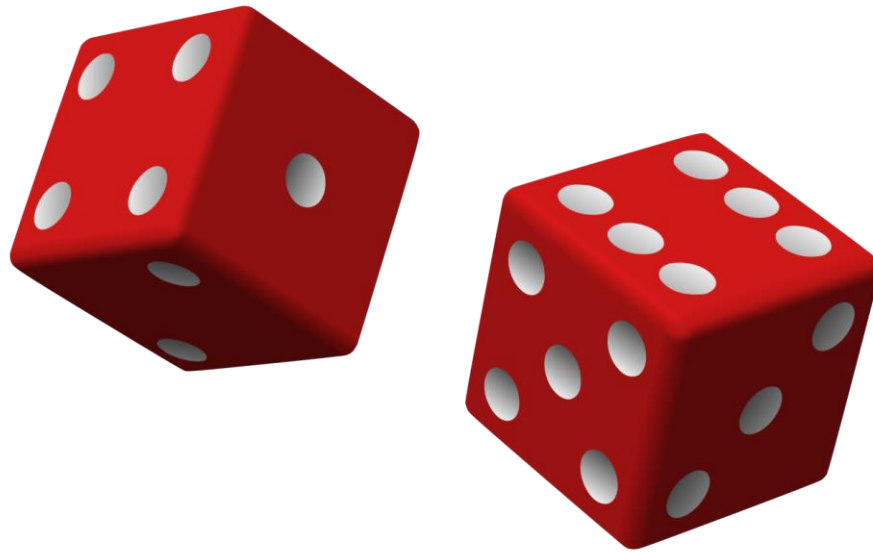
Medications may have been stored in sub optimal conditions.



E.g. Living on boat in Indonesia / off-shore oil rig / Taiwan / relocated to NSW

+ Factors affecting SVR12

- Small sample size bias (chance)



+ Actions

- All individuals who purchased OS DAA have been informed of our experience and encouraged to complete SVR12 test
- All individuals have been offered retreatment with PBS supply.
- Discuss with other centres
 - Via OzHep
 - FixHepC
- Unsure if other services have had similar results

+ FixhepC discussion

- FixhepC treated 448 patients
 - 38 failures (i.e. 92% success rate)
- Slow response in a patient taking body building supplement.
 - BMS published an avoid Taurine warning with DCV
- FixHepC report: Gilead states a 45 day shelf life at 25C/80% relative humidity



+ Conclusion

- Individuals who imported DAA therapy
 - highly motivated
 - purchased at own cost
 - high levels of adherence
- SVR12 rates of imported DAA's
 - 40% achieved SVR12
 - unexpectedly low
- RDH VHS has commenced 245 PBS supplied DAA's
 - 45 SVR12 results completed
 - 100% achieved SVR12
- Explanation for low SVR12 rate remains unclear
 - Batch quality, inadequate drug level
 - Cold chain, storage, climate
 - Manufacturing





Conclusion

- Collection of SVR12 remains important
 - Three individuals did not complete and required recontacting
 - Reported did not plan to follow up SVR12
 - Believing cleared on EOT testing
 - one individual still not done
- In our experience imported DAA's have failed to deliver the expected outcomes





Thank you





Switched PBS & SVR12 pending

- F 63- Gt 1, cirrhotic, Rx Exp: completed 8 weeks (imported) + 16 weeks (PBS) SOF/LED/RBN
 - On Rx viral load: <12 ND
 - EOT viral load: <12 ND
- F 60- Gt 3, cirrhotic, Rx naïve: completed 25 weeks SOF/DCV (one week imported DAA)
 - On Rx viral load: <12 ND
 - EOT viral load: <12 ND
- M 52- Gt 3, cirrhotic, Rx Exp: Completed 8 weeks SOF/DCV/RBN & extended with 24 weeks SOF/DCV (remains on Rx)
 - On Rx viral load: <12 ND
- M 43- Gt 1, nil cirrhosis, naïve: completed 12 weeks SOF/LED
 - EOT SVR12 = <12 ND
 - SVR12: not done

Profile	n=14	
Individuals Imported DAA	Mean Age= 52.5 yrs	
Gender		
Male	9 (64%)	
Female	5 (36%)	
Cirrhosis		Male / Female
Cirrhotic	5 (36%)	2 (40%) / 3 (60%)
Non-Cirrhotic	9 (64%)	7 (78%) / 2 (22%)
Experience		Male / Female
Prior Rx	4 (29%)	3 (75%) / 1 (25%)
Naïve	10 (71%)	6 (60%) / 4 (40%)
Genotypes		Male / Female
G1	6 (42 %)	4 (66%) / 2 (34%)
G2	1 (8 %)	1 (100%) / 0
G3	7 (50 %)	4 (57%) / 3 (43%)

Genotype 1- Patient Results

Non-cirrhotic - Naïve - Rx SOF+LED - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
- M 37	Unk	100%	N	2,097,667 iu/ml	<12 ND	<12 Detected	Detected- PCR
- M 43	Unk	100%	N	880,000 iu/ml	Not done	<12 ND	Pending* (not done)
- M 58	Unk	100%	N	595,927 iu/ml	<12 ND	Not done	Achieved <12 ND
- F 26 (Not FixHepC)	N	100%	N	2,500,000 iu/ml	Not done	<12 ND	Achieved <12 ND
Cirrhotic - Naïve - Rx SOF+LED - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	*SVR 2 Result
- M 59	min	100%	N	14276447 iu/ml	Not done	Not done *ALT normal	Detected 1295387iu/ml *ALT abnormal
Cirrhotic - Exp - Rx SOF+LED+RBV - Duration 24 weeks (OS DAA + PBS) - F 63 (FHC)	ETOH	SR-ADH	AE	Baseline VL	On Rx VL	EOT VL	SVR 12 Result
	N	100%	Y	146022	<12ND	<12 ND	Pending- due 10/2016

Genotype 2- Patient Results

Non-cirrhotic - Naïve - Rx SOF+RBV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
- M 70	Y	100%	N	34481 iu/ml	<12 detected	<12 ND	Achieved <12 ND

Genotype 3- Patient Results

Non-cirrhotic - Naïve - Rx SOF+DCV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
- F 51	N	100%	N	4,333,069	18 iu/ml	<12ND	Detected
- M 58	Y	Mostly	N	7,479,188	<12ND	<12ND	Achieved <12 ND
Non-cirrhotic - Experience - Rx SOF+DCV - Duration 12 weeks	ETOH	SR-ADH	AE	Baseline VL	ON Rx VL	EOT VL	SVR 12 Result
-DM M 50 (FHC)	N	100%	N	770,000 iu/ml	<12 Detected	<12ND	Detected
-IB M 53	N	100%	N	16,550,529 iu/ml	14389 iu/ml	8133365 iu/ml	Detected

Genotype 3- Patient Results

Cirrhotic

- Naïve
- Rx SOF+DCV
- Duration 24 weeks

-F 55 (Not FixHepC)

DO F 60
(25 weeks of Rx –
1 O/S DAA + 24
weeks PBS)

ETOH

SR-ADH

AE

Baseline VL

ON Rx VL

EOT VL

SVR 12 Result

N

100%

Y

1603201 iu/ml

74 iu/ml

Interstate

Detected

Y

100%

N

1996662 iu/ml

<12ND

<12ND

Pending- December 2016

Cirrhotic

- Exp
- Rx SOF+DCV+RBV
- Duration 24 weeks

TB M 52 (FHC)
(32 weeks of Rx- 8
weeks O/S DAA
with RBV + 24
weeks PBS
SOF+DCV (no
RBV)

ETOH

SR-ADH

AE

Baseline VL

On Rx VL

EOT VL

SVR 12 Result

N

100%

N

3,202,122 iu/ml

<12ND

Pending-
October

Pending January 2017



Outcomes of FixHepC Supplied Therapy by Batch n= 10

