Current Management of HCV and Experience with DAAs in Myanmar 2017

Professor Khin Maung Win, FRCP (Edin)

Honorary Professor

Department of Hepatology

University of Medicine 1

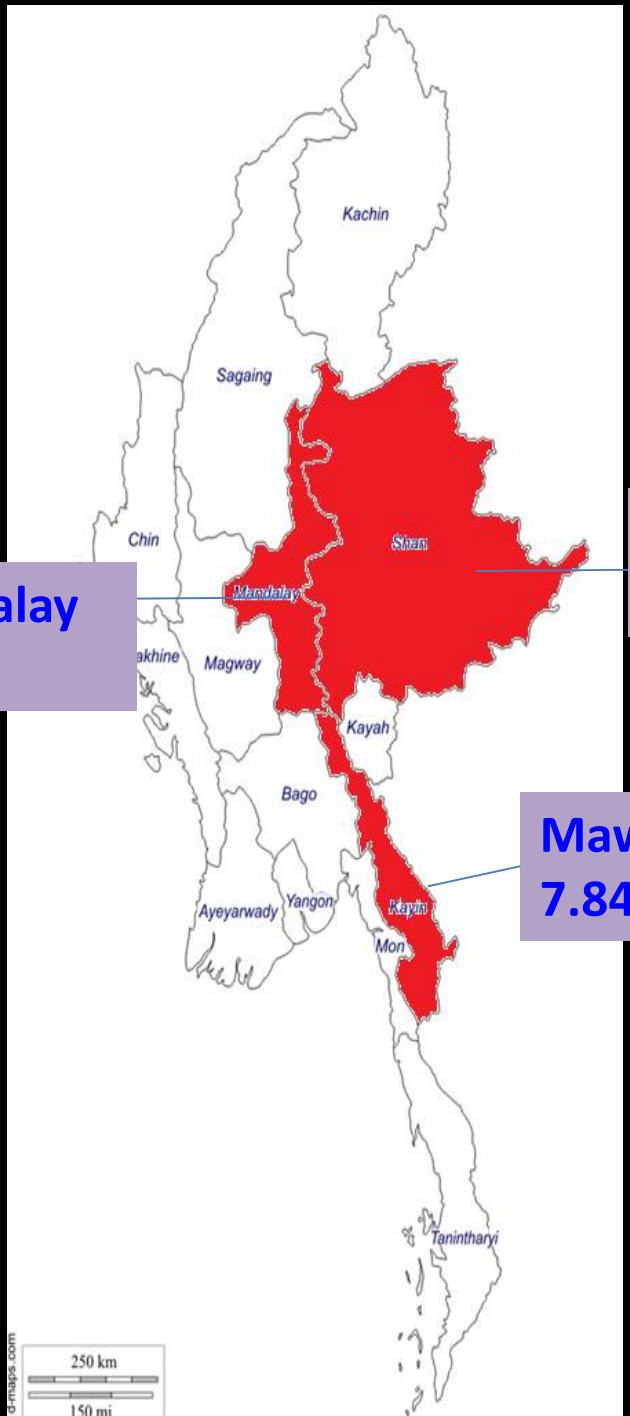
Ministry of Health and Sports

Yangon, Myanmar

Disclosure

I have nothing to disclose.

HCV Burden in Myanmar



Mandalay 7.7%

Lashio 5.03%

Mawlamyaing 7.84%

- **Prevalence of Hepatitis in general population = 2.65%** (0.32 – 10.34)
- 1.3 million have a history of HCV infection (anti-HCV positive)

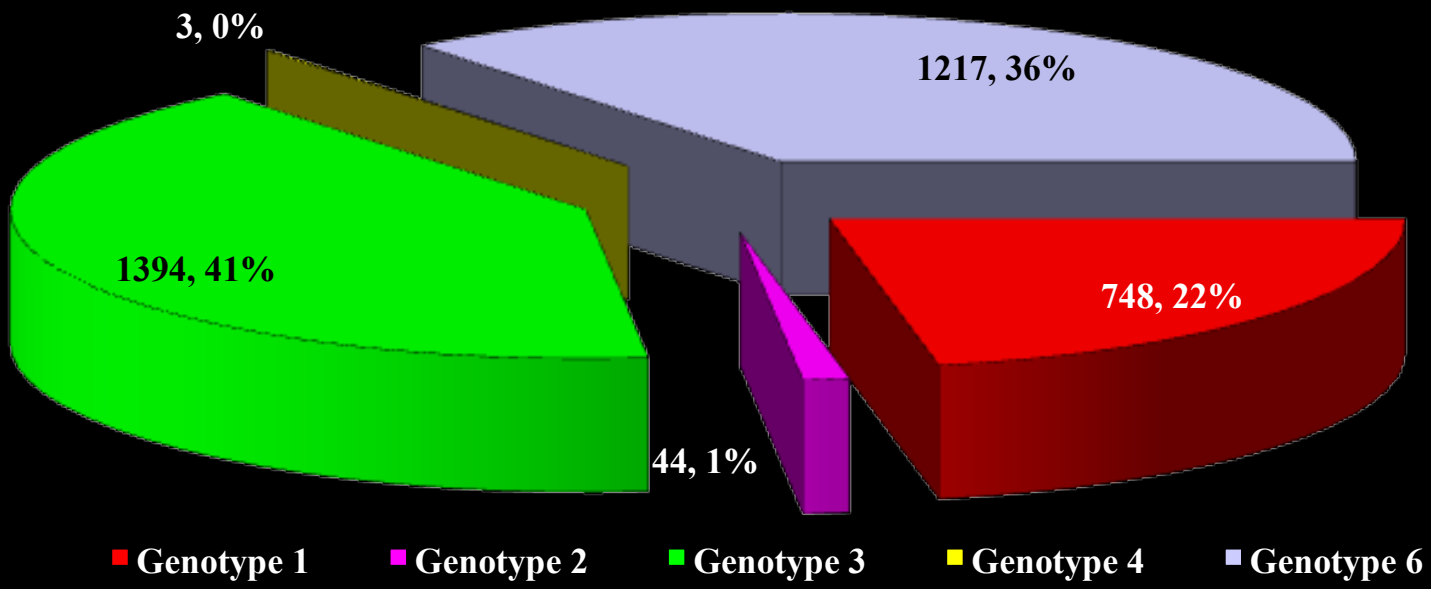
National Prevalence Survey for Hepatitis B and C, 2015

Disease Burden of Viral Hepatitis in Myanmar

Prevalence	Population	Prevalence rate
Mono-infection of HBV	* General population (2015) **Among blood donors (2015) * Multi-transfused patients * Patients undergoing hemodialysis # PWID	6.51% 3.7% 6.1% 4.9% 8.2%
Mono-infection of HCV	* General population (2015) **Among blood donors (2015) * Multi-transfused patients * Patients undergoing hemodialysis # PWID	2.65% 0.71% 3.1% 12.8% 58.9%
Co-infection	# HIV/ HBV # HIV/ HCV # HIV & HBV/ HCV	2.2% 20.1% 20.7%

* DMR National survey (2015) ** Annual report of National Blood Bank (2015)
# IBBS study among PWID (2014)

HCV Genotyping by Versant (LiPA)
2009 & 2015 December
Total number = 3406

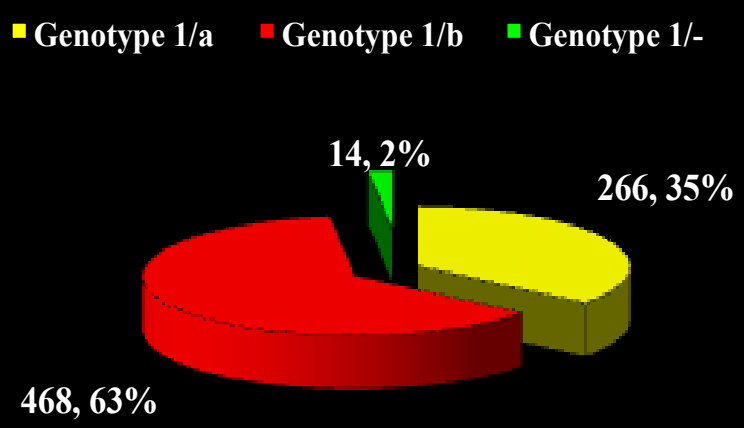


Major Genotypes in Myanmar

- G 3 - 1394 (41 %)
- G 6 - 1217 (36 %)
- G 1 - 748 (22 %)
- G 2 - 44 (1 %)
- G4 - 3 (0 %)

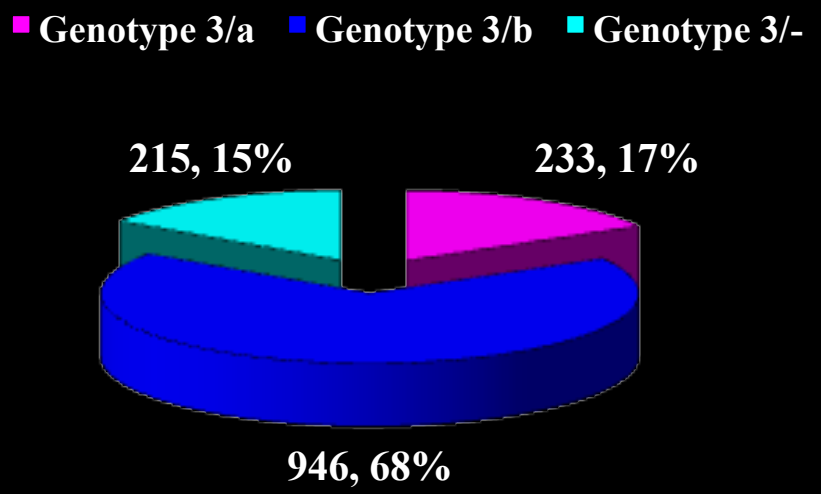
HCV Genotyping
Versant (LiPA 2.0)
2009 to 2015
Genotype 1
Total number = 748

Subtype 1b dominant



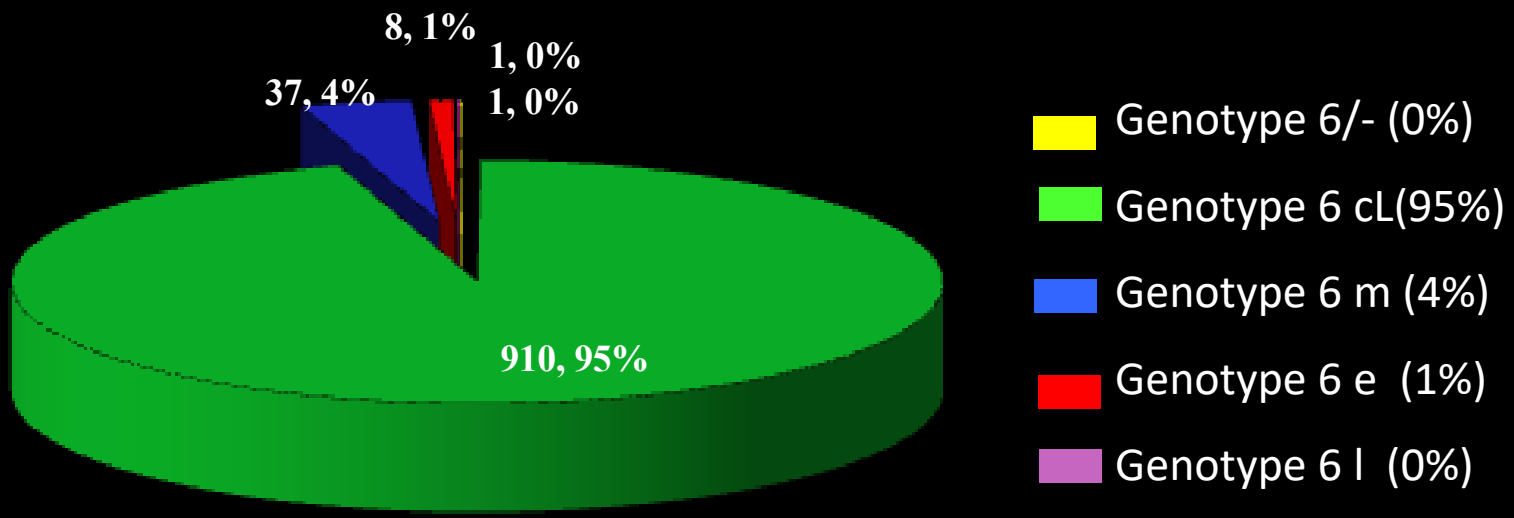
HCV Genotyping
Versant (LiPA 2.0)
from 2009 to 2015
Genotype 3
Total number =1394

Subtype 3b dominant

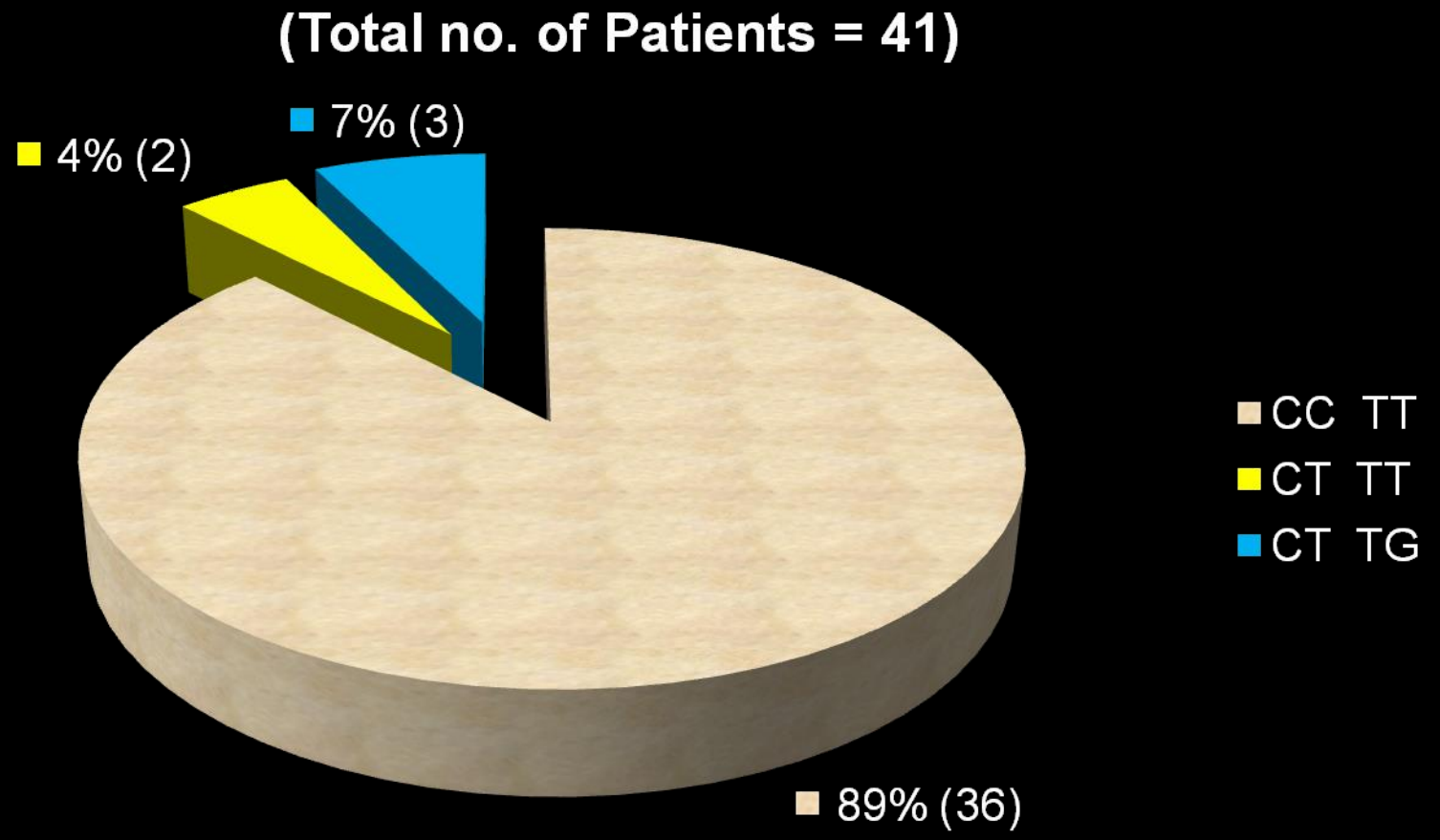


HCV Genotyping
Versant (LiPA 2.0)
2009 to 2015
Genotype 6
Total number = 957

Subtype 6 cL dominant

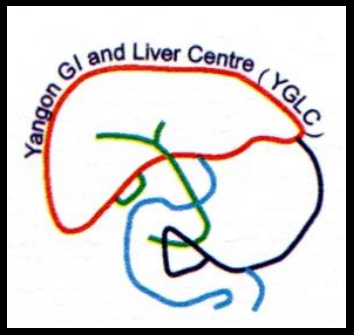


IL28B Gene Polymorphisms in Myanmar Patients with Chronic HCV Infection Genotype 1



Available Generic DAAs in Myanmar

DAAs	Available Since	Myanmar FDA Approvel
Sofosbuvir	(2014)	Myanmar FDA Approved
Sofosbuvir + Ledipasvir	(2015)	Myanmar FDA Approved
Daclatasvir	(Early 2016)	Myanmar FDA Approved
Sofosbuvir + Velpatasvir	(Late 2016)	Myanmar FDA approved



Real life data of the 552 Myanmar Patients with Chronic HCV Infection treated by DAAs

1.12.2015 to 1.12.2016

Baseline characteristics 1

Myanmar	SR (SOF-RBV)	SPR (SOF-IFN-RBV)	SD (SOF-DCV)	SDR (SOF-DCV-RBV)	SL (SOF-LDV)	SLR (SOF/LDV/RBV)	TOTAL
Number	134	161	40	8	171	38	552
Gender M	50 (37.3)	72 (44.7)	15 (37.5)	3 (37.5)	62 (36.3)	18 (47.4)	220 (39.9)
Age	55±10	49±10	55±13	55±5	55±13	54±10	53±12
Cirrhotic	58 (43.3)	33 (20.5)	18 (45.0)	6 (75.0)	51 (29.8)	19 (50)	185 (33.5)
Naïve Treated	108 (80.6) 26 (19.4)	128 (79.5) 33 (20.5)	37 (92.5) 3 (7.5)	1 (12.5) 7 (87.5)	152 (88.9) 19 (11.1)	19 (50.0) 19 (50.0)	445 (80.6) 107 (19.4)
Genotype							
1	17 (12.7)	32 (19.9)	0	0	71 (41.5)	14 (36.8)	134 (24.3)
2	1 (0.7)	3 (1.9)	0	0	2 (1.2)	0	6 (1.1)
3	84 (62.7)	77 (47.8)	40 (100)	8 (100)	0	0	209 (37.9)
6	24 (17.9)	44 (27.3)	0	0	85 (49.7)	24 (63.2)	177 (32.1)
Indeterminate	8 (6.0)	5 (3.1)	0	0	13 (7.6)	0	26 (4.7)
HCV RNA (10^6 IU/ml)	5.0±17.3	4.0±8.2	4.1±8.6	3.2±3.4	4.0±8.0	4.3±11.3	4.3±11.2

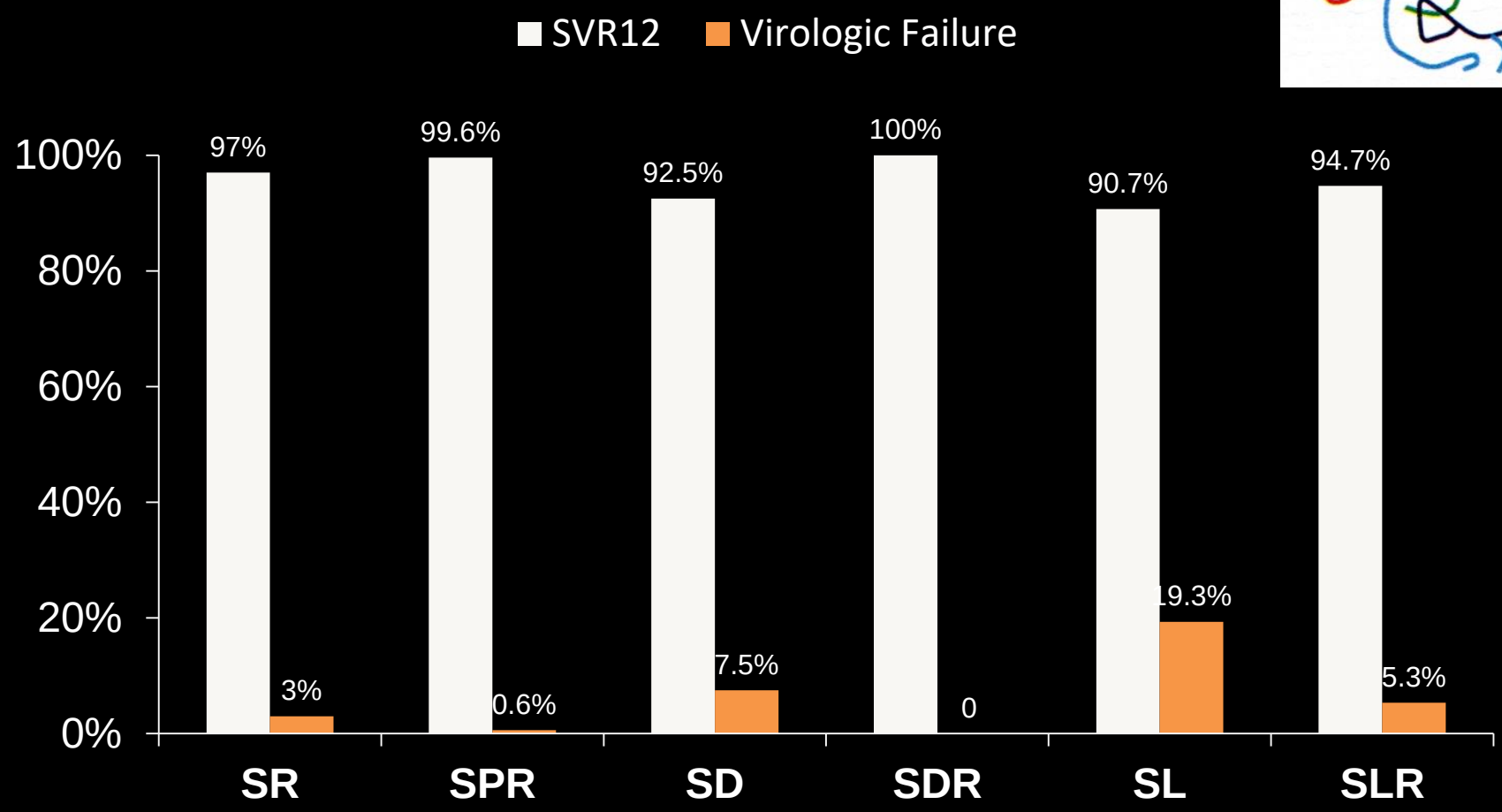
Categorical variables are in percent and continuous variables are in ±standard deviation.

Baseline characteristics 2

Myanmar	SR (SOF-RBV)	SPR (SOF-IFN-RBV)	SD (SOF-DCV)	SDR (SOF-DCV-RBV)	SL (SOF-LDV)	SLR (SOF/LDV/RBV)	TOTAL
Number	134	161	40	8	171	38	552
Albumin g/L	33.8±5.7	36.2±5.0	34.3±4.2	34.9±4.9	37.4±26.8	33.2±5.3	35.6±15.6
Bilirubin (umol/l)							
AST (U/L)	70±88	48±42	53±72	54±36	50±105	48±34	54±79
ALT (U/L)	75±87	72±95	66±97	58±48	58±70	50±35	66±82
Hb (g/L)	12.2±1.7	12.5±2.0	12.5±2.0	12.9±1.1	13.4±8.5	12.3±1.8	12.7±5.0
WBC (10^9/L)	6.5±2.1	7.8±7.6	6.8±2.1	6.0±1.9	7.1±2.1	6.9±2.7	7.1±4.5
Platelet count (10^9/L)	162±70	203±62	187±62	162±90	206±68	188±91	191±70
INR	1.1±1.1	1.8±7.8	1.2±1.4	1.0±0.2	1.1±1.7	1.3±1.5	1.3±4.3
AFP	35±260	9±17	6±3	7±6	8±16	10±15	15±129

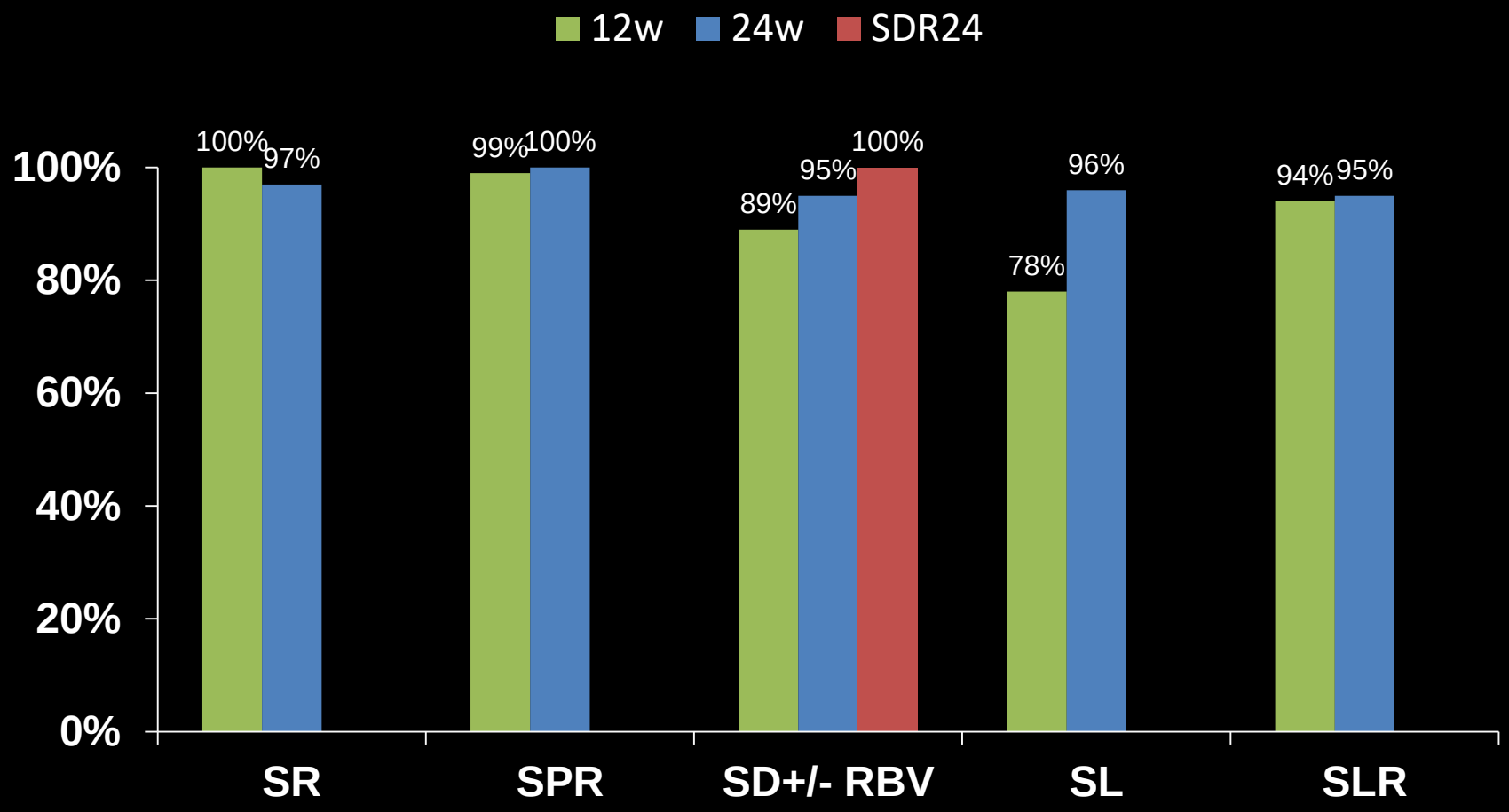
Categorical variables are in percent and continuous variables are in mean±standard deviation.

SVR12 by Treatment



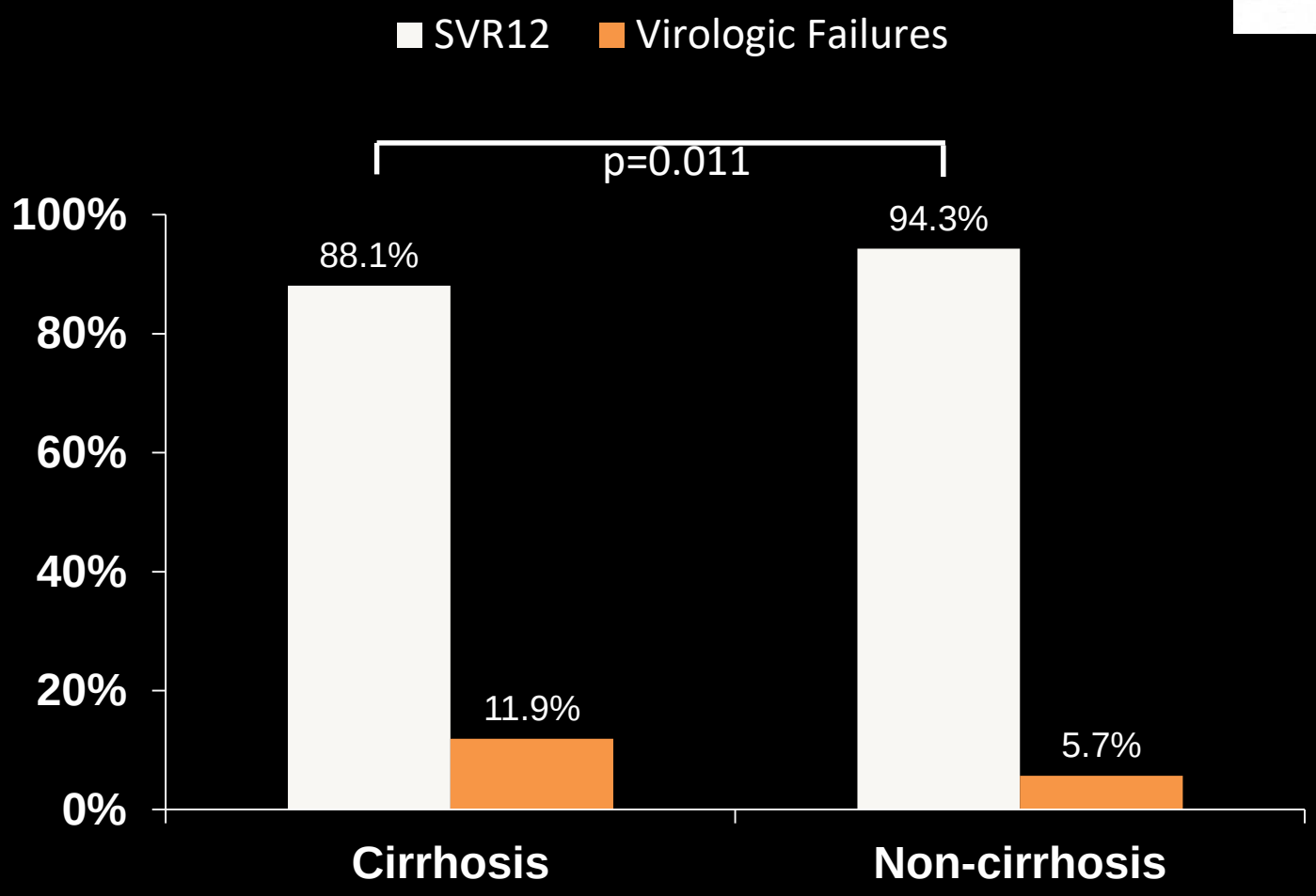
SR=Sofosbuvir/Ribavirin; SPR=Sofosbuvir/peginterferon/ribavirin;
SD=Sofosbuvir/Daclatasvir; SDR=Sofosbuvir/Daclatasvir/Ribavirin;
SL=Sofosbuvir/Ledivaspvir; SLR= Sofosbuvir/Ledivaspvir/Ribavirin

SVR12 by duration of therapy

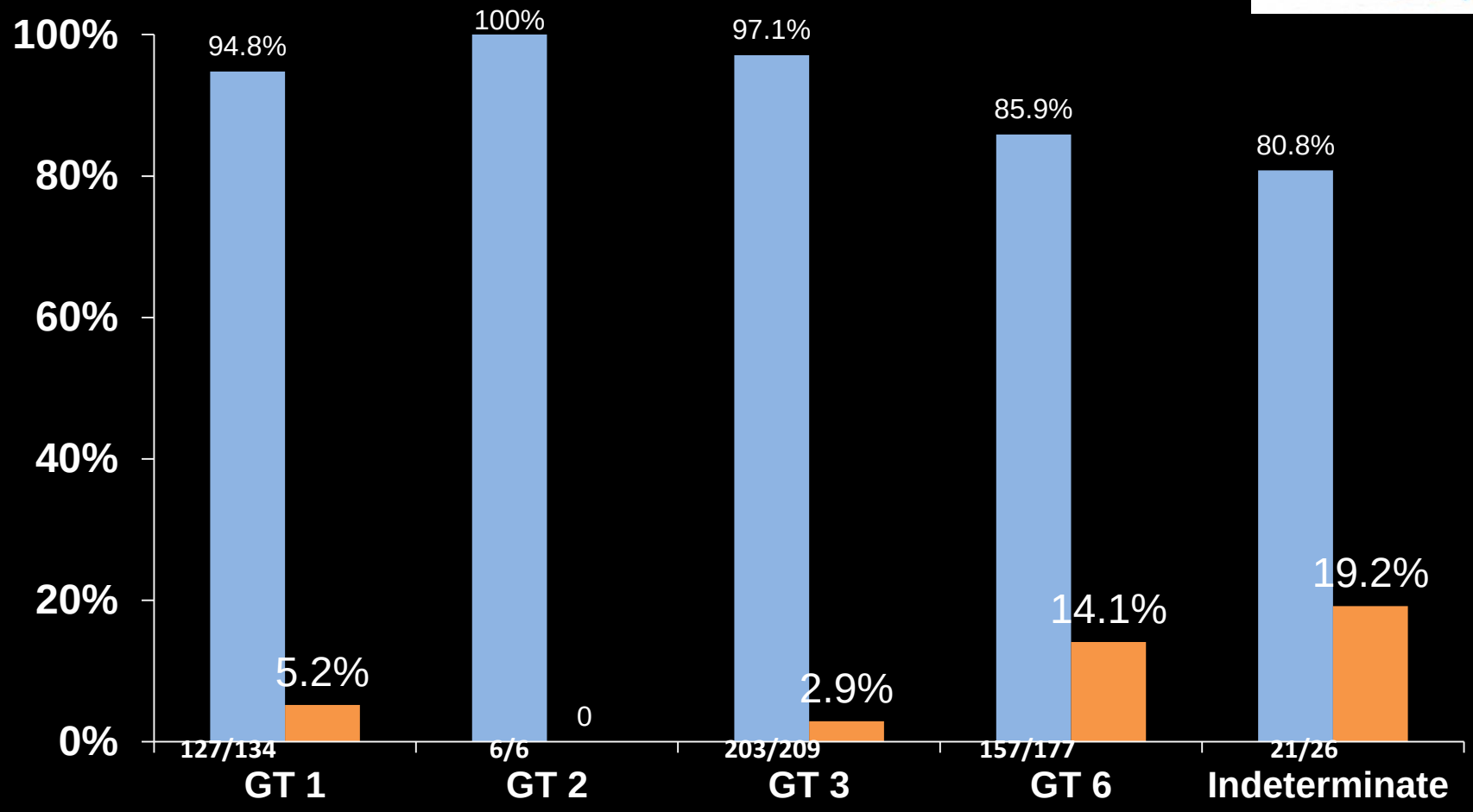


SR=Sofosbuvir/Ribavirin; SPR=Sofosbuvir/peginterferon/ribavirin;
SD=Sofosbuvir/Daclatasvir; SDR=Sofosbuvir/Daclatasvir/Ribavirin;
SL=Sofosbuvir/Ledivaspvir; SLR= Sofosbuvir/Ledivaspvir/Ribavirin

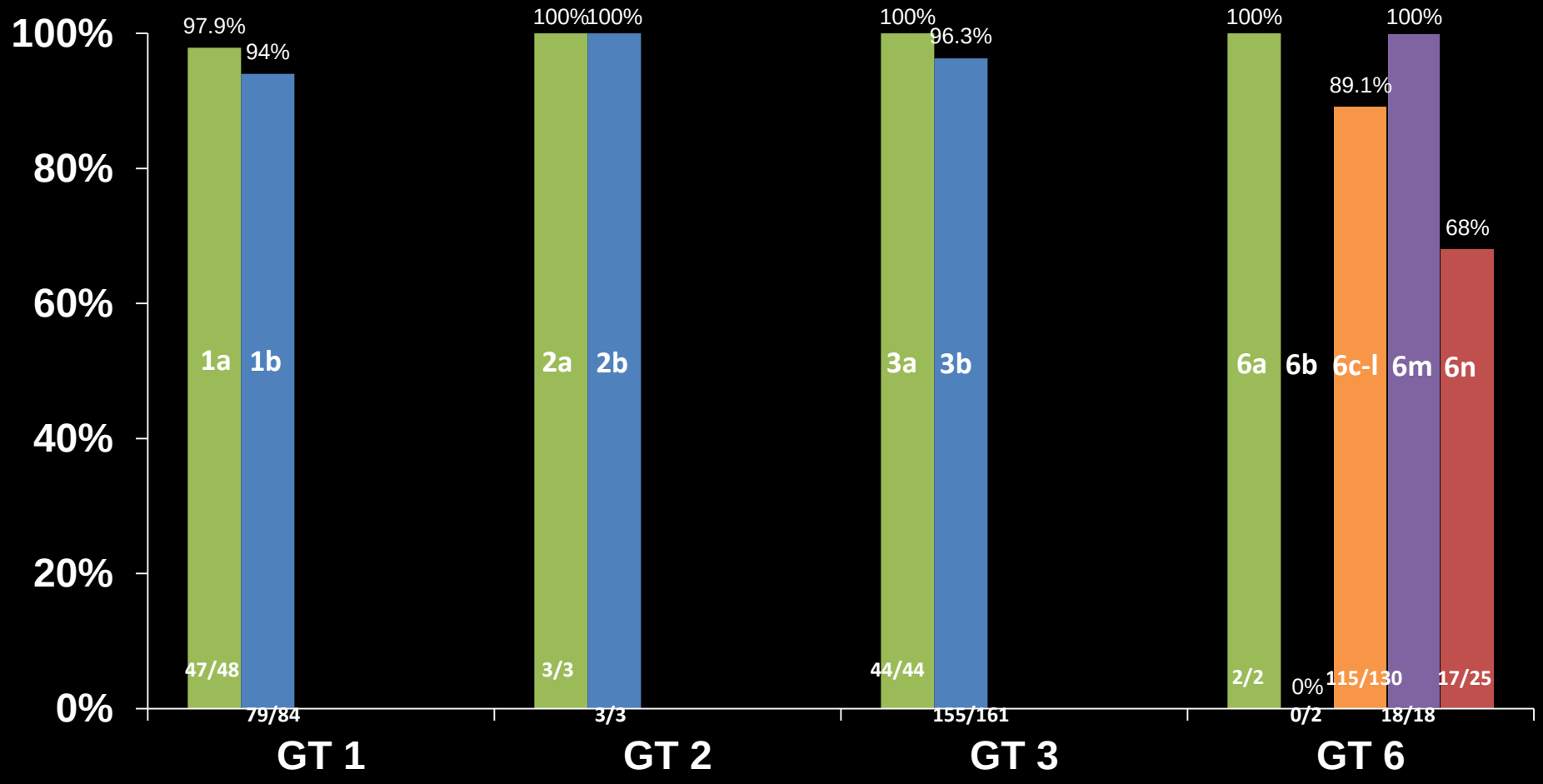
SVR12 by cirrhosis



SVR12 by Genotype

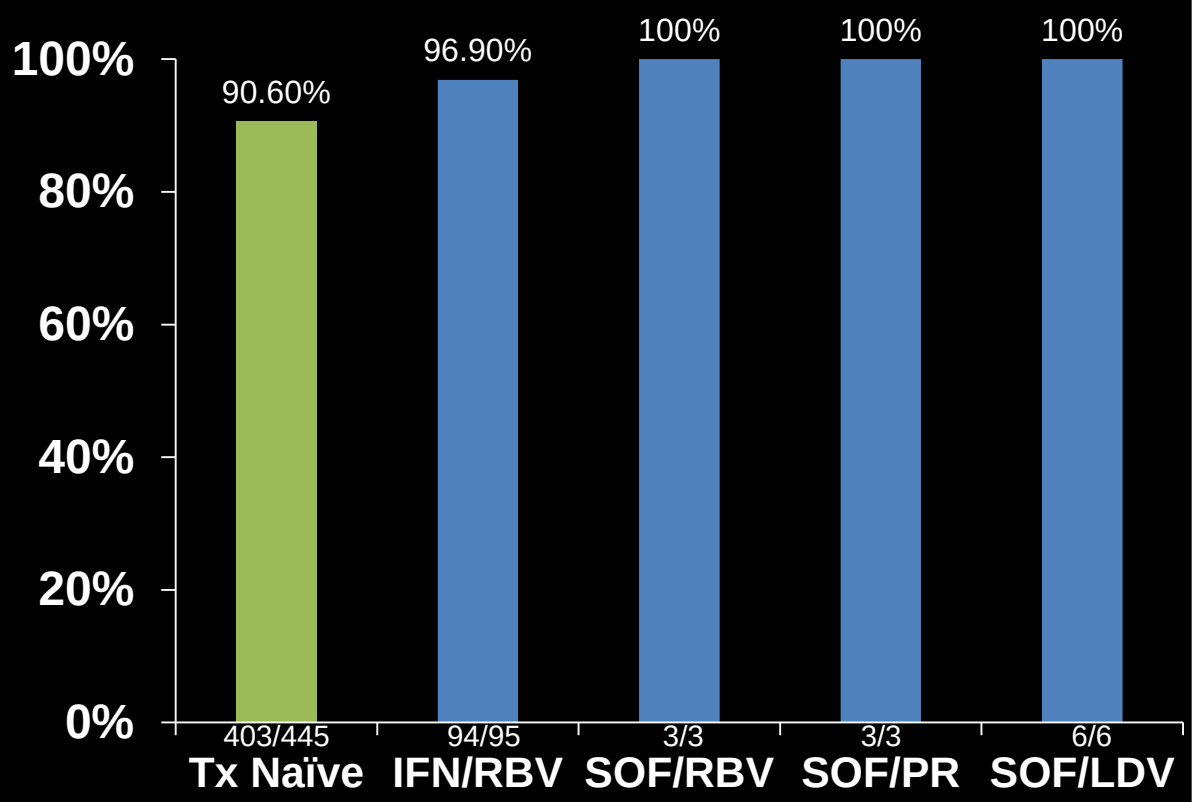


SVR12 by Sub-genotype

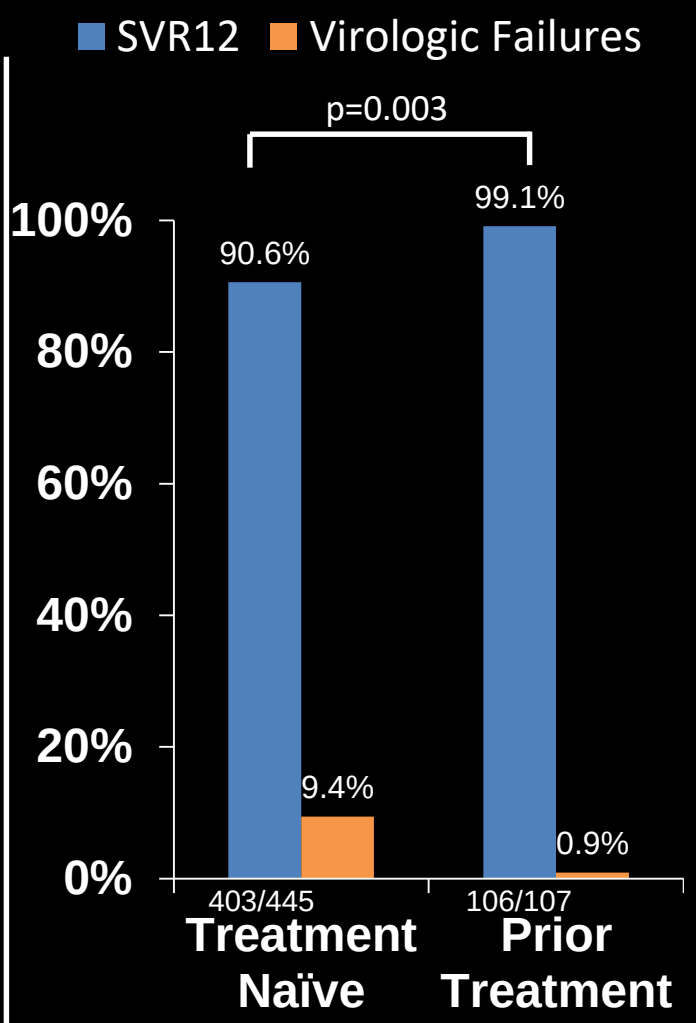


SVR12 by prior therapy

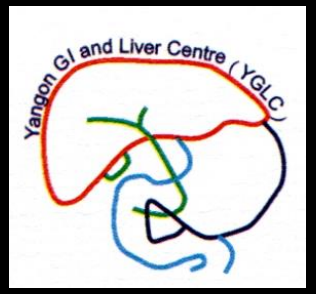
SVR12 by prior type of prior therapy



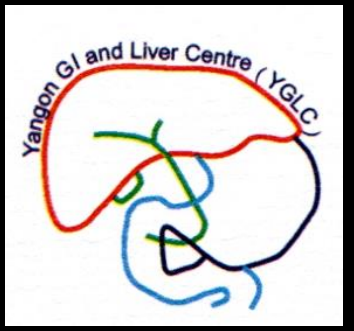
SVR12: Tx naïve vs prior therapy



Conclusions



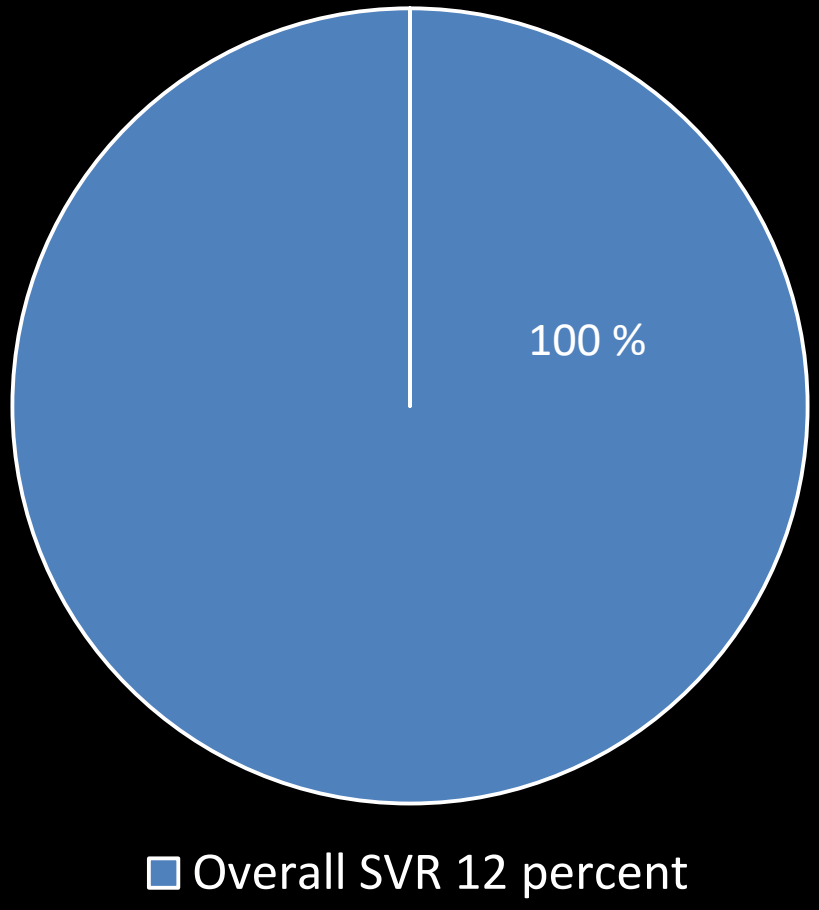
- A total of 552 HCV patients received DAA therapy in Myanmar
- The most common genotypes treated were GT3(37.9%), GT6(32.1%), and GT1(24.3%), GTInd (4.7%), GT2 (1.1%)
- Approximately 33% were cirrhotic and 80.6% were treatment naïve
- Treatments included 12 or 24 weeks of
  - SOF/RBV
  - SOF/PR
  - SOF/DCV±RBV
  - SOF/LDV±RBV
- SVR12 were >90% in most groups of patients and genotypes, with exception of
  - GT6 overall SVR 85.9% with GT6c-l SVR12 89%, and GT6n SVR12 68%
- Cirrhotics had a slightly lower SVR12 of
  - 88.1% compared to
- Non cirrhotic of 94.3%



Preliminary Report of Real Life Experience of 186 Cases of CHC treated with SOF/VEL/RBV x 12wks Without genotyping and Fibroscan measurement

September, 2016 – June, 2017

SVR12 % in SOF/VEL/RBV 12 weeks treatment of chronic HCV infection in Myanmar patients without genotyping, and Fibroscan measurement



N.B All patients are ribavirin eligible and there are no serious adverse effects requiring stopping of ribavirin.

Use of DAAs in Resource Limited Situations

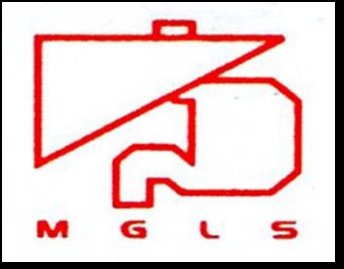
- To have the optimal SVR results with the treatment of chronic HCV infection using DAAs it is necessary to know the;
  - Genotype
  - Fibrosis score
  - Measurement of Viral Load at the designated time points
- However, in resource limited situations where the above mentioned parameters can not be performed, to get the best results special unique treatment regimen should be adopted

Use of DAAs in Resource Limited Situations (Special Regimen)

- Myanmar GI & Liver Society clinical practice treatment guidelines (2017) recommend the following regimen for those who cannot afford genotype testing or Fibroscan;
  - ***SOF/VEL/RBV 12 weeks***
- This regimen is also approved by Afro-Asian Advisory Board Meeting, Satellite Meeting of EASL 2017 (April, 2017 in Netherlands)

Conclusion

- Real world generic DAAs experiences in Myanmar
  - Cheap compared to the prices in the developed countries
  - Free from adverse effects
  - Very effective and achieving SVR rates above 90% in all the cases.
- In resource-limited situations like Myanmar, the following clinical practice guidelines for the treatment of CHC is proposed;
  - Pangenotypic SOF/VEL can be combined with Ribavirin in cases of lack of genotype and fibrosis score.
  - In those cases SOF/VEL/RBV 12 weeks can result in 100% SVR rates
  - Myanmar patients can tolerate RBV very well.
  - Viral load determination can be done pre-treatment and 12 weeks after stopping the treatment.
- It is highly recommended to practice such special treatment regimen in resource limited countries like Myanmar.

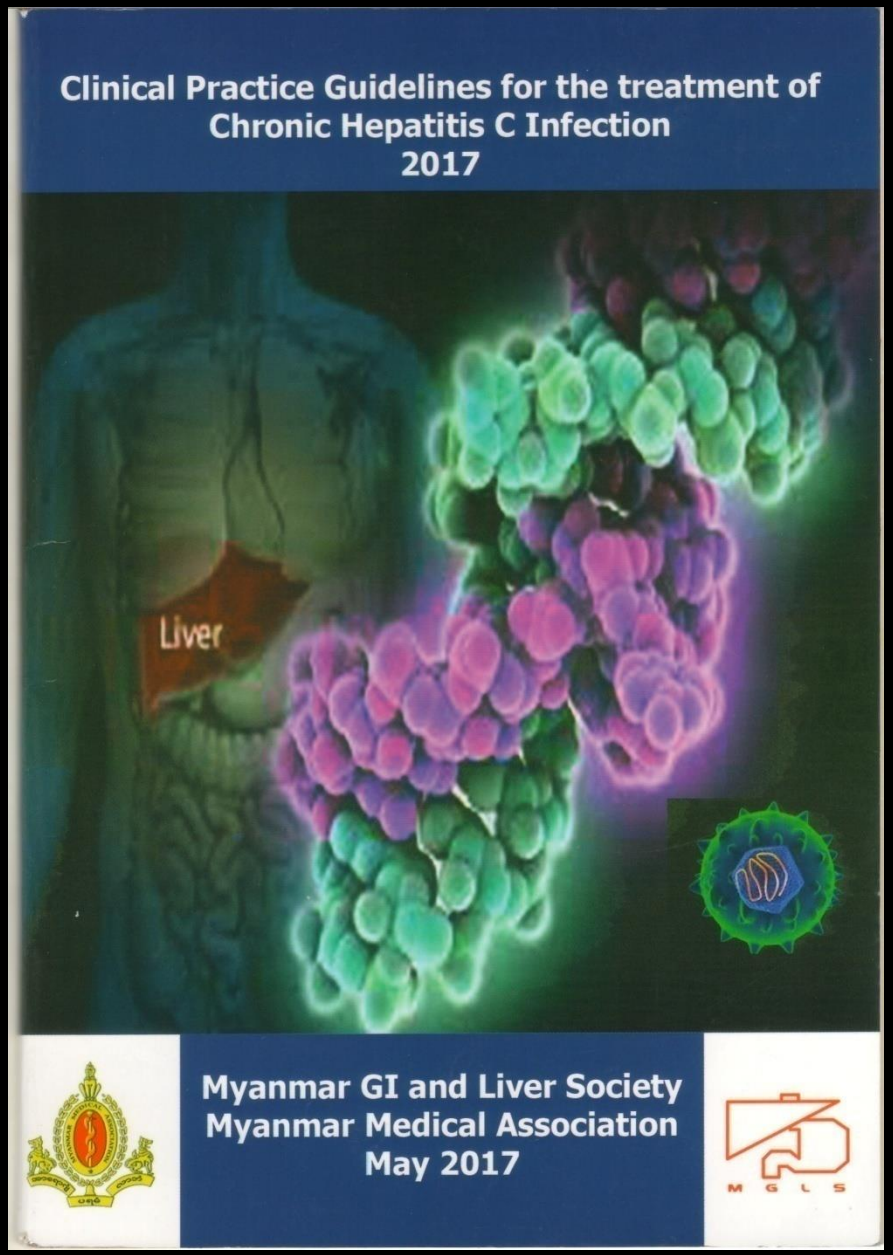


Myanmar Gastroenterology & Liver Society
Myanmar Medical Association

Myanmar Guidelines For Treatment of Hepatitis C Infection May 2017

Myanmar Gastroenterology & Liver Society
Myanmar Medical Association

Myanmar Hepatitis C Treatment Guidelines Revised in 2017 May



Genotype 1 (a and b)

Genotype 1a patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*
SOF/LED	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *AASLD (Class I, Level A)* *EASL (A1)*
SOF/DCV	**12 weeks** *AASLD (Class I, Level B)* *EASL (B1)*	**12 weeks + RBV** *EASL (C2)* **(24 weeks if RBV intolerant)** *EASL (B1)*	**24 weeks ± RBV** *AASLD (Class IIa, Level B)*	**24 weeks ± RBV** *AASLD (Class IIa, Level B)* *EASL (B1)*

Genotype 1b patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*
SOF/LED	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*
SOF/DCV	**12 weeks** *AASLD (Class I, Level B)* *EASL (B1)*	**12 weeks** *AASLD (Class I, Level B)* *EASL (B1)*	**24 weeks ± RBV** *AASLD (Class IIa, Level B)*	**24 weeks ± RBV** *AASLD (Class IIa, Level B)*

Genotype 1 DAA experienced treatment options

Recommended regimen / Past regimen	SOF/VEL	SOF/LED	SOF/DCV
SOF/RBV ± PEG IFN	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*
NS5A inhibitors (DCV or LED)	**Patients without an urgent needs for treatment can wait until more data and/or alternative therapeutic options become available** *EASL (A1)* However according to personal experiences in real life patients, SOF/VEL + RBV for 24 weeks may be tried.		

Genotype 2

Genotype 2 patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	12 weeks *AASLD (Class I, Level A)* *EASL (A1)*	12 weeks *AASLD (Class I, Level A)* *EASL (A1)*	12 weeks *AASLD (Class I, Level A)* *EASL (A1)*	12 weeks *AASLD (Class I, Level A)* *EASL (A1)*
SOF/DCV	12 weeks *AASLD (Class II, Level B)* *EASL (B1)*	12 weeks *AASLD (Class II, Level B)* *EASL (B1)*	12 weeks *EASL (B1)*	12 weeks *EASL (B1)*

Genotype 2 DAA experienced treatment options

Recommended regimen / Past regimen	SOF/VEL	SOF/DCV
SOF/RBV ± PEG IFN	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**24 weeks + RBV** **(if RBV tolerant)** regardless of cirrhosis status *AASLD (Class IIa, Level C)*
NS5A inhibitors (DCV or LED)	**24 weeks + RBV** *EASL (B1)*	-

Genotype 3 (a and b)

Genotype 3 patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (C1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (C1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *AASLD (Class I, Level B)* *EASL (C1)*
SOF/DCV	**12 weeks** *AASLD (Class I, Level A)* *EASL (B1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (C1)*	**24 weeks + RBV (if RBV tolerant)** *AASLD (Class IIa, Level A)* *EASL (C1)*	**24 weeks + RBV (if RBV tolerant)** *AASLD (Class IIa, Level A)* *EASL (C1)*

Genotype 3 DAA experienced treatment options

Recommended regimen / Past regimen	SOF/VEL	SOF/DCV
SOF/RBV ± PEG IFN	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**24 weeks + RBV (if RBV tolerant)** regardless of cirrhosis status *AASLD (Class IIa, Level C)*
NS5A inhibitors (DCV or LED)	**24 weeks + RBV** *EASL (B1)*	-

Genotype 4

Genotype 4 patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*
SOF/LED	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (B1)*	**12 weeks** *AASLD (Class I, Level A)* *EASL (A1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *AASLD (Class I, Level A)* *EASL (B1)*
SOF/DCV	**12 weeks** *EASL (B1)*	**12 weeks+ RBV (24 weeks if RBV intolerant)** *EASL (B1)*	**12 weeks** *EASL (B1)*	**12 weeks + RBV (24 weeks if RBV intolerant)** *EASL (B1)*

Genotype 4 DAA experienced treatment options

Recommended regimen / Past regimen	SOF/VEL	SOF/LED	SOF/DCV
SOF/RBV ± PEG IFN	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*	**12 weeks + RBV** F0 - F2 (No COL) OR **24 weeks + RBV** F3-F4 (COL) *EASL (B1)*
NS5A inhibitors (DCV or LED)	**Patients without an urgent needs for treatment can wait until more data and/or alternative therapeutic options become available** *EASL (A1)*		

Genotype 5 and 6

Genotype 5 or 6 patients without cirrhosis and with compensated cirrhosis

Combination regimen	No cirrhosis		Compensated cirrhosis	
	Treatment naive	Treatment experienced (Peg: + Ribavirin)	Treatment naive	Treatment experienced (Peg: + Ribavirin)
SOF/VEL	12 weeks *EASL (A1)*	12 weeks *EASL (A1)*	12 weeks *EASL (A1)*	12 weeks *EASL (A1)*
SOF/LED	12 weeks *EASL (B1)*	12 weeks + RBV (24 weeks if RBV intolerant) *EASL (B1)*	12 weeks *EASL (B1)*	12 weeks + RBV (24 weeks if RBV intolerant) *EASL (B1)*
SOF/DCV	12 weeks *EASL (B2)*	12 weeks+ RBV (24 weeks if RBV intolerant) *EASL (B2)*	12 weeks *EASL (B2)*	12 weeks + RBV (24 weeks if RBV intolerant) *EASL (B2)*

Genotype 5 or 6 DAA experienced treatment options

Recommended regimen / Past regimen	SOF/VEL	SOF/LED	SOF/DCV
SOF/RBV ± PEG IFN	12 weeks + RBV F0 - F2 (No COL) OR 24 weeks + RBV F3-F4 (COL) *EASL (B1)*	12 weeks + RBV F0 - F2 (No COL) OR 24 weeks + RBV F3-F4 (COL) *EASL (B1)*	12 weeks + RBV F0 - F2 (No COL) OR 24 weeks + RBV F3-F4 (COL) *EASL (B1)*
NS5A inhibitors (DCV or LED)	24 weeks + RBV *EASL (B1)*		

Thank you