

Viral hepatitis treatment for people with HIV in Asia

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HIV/HCV coinfection: Public Health Challenges in Asia

- prevalence, HCV genotype distribution
- HCV treatment outcome in Asia
- Challenges/unmet need in providing treatment and care

Hepatitis C regional prevalence 2010

Region	Anti-HCV(%)	No.HCV-infected	Country	Anti-HCV(%)	No.HCV-infected
Africa	3.2	28,100,000	China	2.2	29,791,212
America	1.5	14,000,000	India	1.5	18,216,960
Asia	2.1	83,000,000	Philippines	2.2	1,932,854
Australia and Oceania	1.2	400,000	Thailand	2.2	1,499,058
Europe	2.3	17,500,000	Vietnam	1	835,360
Middle East	4.7	16,000,000	Malaysia	1.5	397,515
Total	2.35	159,000,000	South Korea	1.68	823,956
Egypt	14%	N=11,826,360	Mynmar	1	505,190
Russia	4.1%	N=5,796,498	Laos	1.1	70,796

Very low awareness/knowledge of HCV status among several risk groups and providers

China: 2006 survey, HCV prevalence in mainland 0.43. Cui Y. JGH 2013

Lavanchy D. Clin Microbiol Infect 2011;17:107-115

Burden of HIV/HCV in Asia

Country	N	Anti-HCV(%)	
India ¹	16124	3.52	
India ²	250	1.2	CSW
Indonesia ³	126	34.1	PWID
Indonesia ⁴	375	4	
Cambodia ⁵	3089	5.3	
Thailand ⁶	700	3.3	
Thailand ⁷	692	7.2	
Thailand ⁸	529	7.8	
Myanmar ⁹	11,032	5.3	

No HCV RNA performed,
No fibrosis assessment

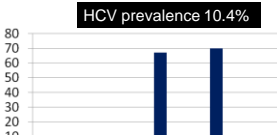
Prevalence of chronic HCV
requiring HCV treatment
has not been
comprehensively estimated

3.5 million HIV
32 million HCV

1. Nagmoti MB, Int J STD AIDS. 2012;23(10):e14-5
2. Praseeda SD J Clin Diagn Res. 2013;7(2):234-7.
3. Araggrowati N, J Med Virol. 2012;84(6):927-45
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5. Van Orienven J Plos one. 2014; 9(2): e88552
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7. Law WPAIDS 2004; 18(8):1169-77
8. Sunkanuparth S. J Med Assoc Thai. 2004;87(11):1349-54
9. Zaw SK Trop Doct.2013;43(3):113-6

HCV prevalence in Treat Asia HIV Database (N=1469) in 2005¹

2979 HIV , 12 countries
49% had HCV testing
44 PWID (5%)



March 2012, N 6,360 in TAHOD:
 -65.3% had HCV testing.
 -17.7% had positive HCV Ab.
 -Only 4.4% of those had received HCV PCR testing.
 -43.8% were found to have positive HCV RNA.
 -Only very few had received treatment.

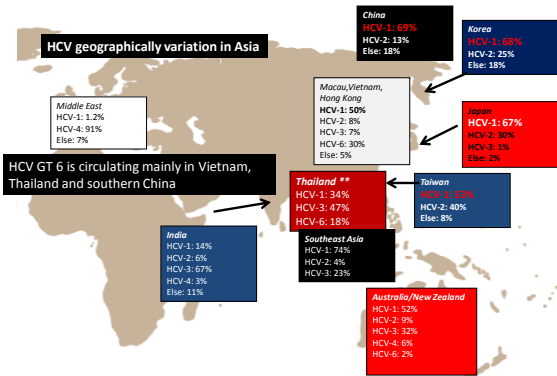
Estimated 2-9 M PWID in Asia

Underestimation of HCV coinfection
and low number of PWID in HIV
treatment and Care program
Expensive, inadequate HCV RNA

HCV in MSM : Asia

- 753 HIV-infected MSM with antiHCV negative
- 21 (2.8%), incidence of 9.35 per 1000PY
- The incidence increased overtime
 - 0 per 1000PY in 2005-2006
 - 3.0 per 1000PY in 2007-2008
 - 7.7 per 1000PY in 2009-2010
 - 24.9 per 1000PY in 2011-2012
- Only 4 were PWID
- Illicit drug use was associated with incident HCV (HR3; 95% CI 1.092-8.275, p=0.033)

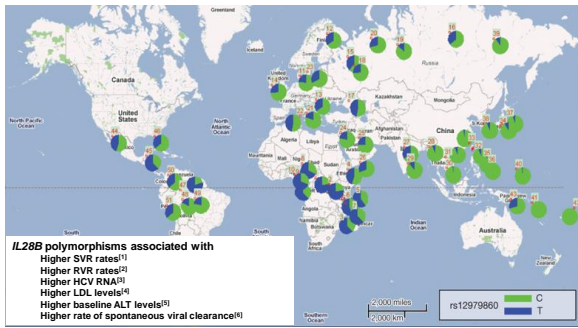
Nishijima T. JAIDS. 2014; 65(2):213-217



Yu ML Hepatology 2009;24:336-345

**Avihingsanon et al. J of gastroenterology and hepatology 2014

Favorable *IL28B* rs12979860 CC Genotype in Asia



1 Ge D, et al. Nature. 2009;461:399-401. 2 Mangia A, et al. AASLD 2010. Abstract 897. 3 Liu L, et al. AASLD 2010. Abstract 231. 4 Saito H, et al. AASLD 2010. Abstract 732. 5. Thompson AJ, et al. AASLD 2010. Abstract 1893. 6. Thomas DL, et al. Nature. 2009;461:798-801.

IL-28b (rs12979860), and HCV viral load between 130HIV/HCV and 331 HCV mono, Thailand : **GT3:47% ; GT1, 34% GT6:18%**

	Total	HIV/HCV	HCV mono	P
IL-28b (%)				0.514
C/C	86.6	88.3	84.7	
C/T	11	10.6	11.8	
T/T	2.2	1	3.5	
HCV RNA Median (IQR)	6.2(5.6-6.9)	6.7(5.6-7.3)	5.8(5.6, 6.5)	<0.001
HCV RNA > 800,000 IU/ml				.01
FibroScan, PKa				.01
<7.1 kPa, N(%)	220 (50.1)	33 (30.6)	187(56.5)	<0.001
7.2-9.4 kPa, N (%)	91(20.7)	30 (27.8)	61(18.4)	
9.5- 14 kPa, N (%)	60 (13.8)	19(17.6)	41 (12.4)	
>14 kPa, N(%)	68 (15.5)	26 (24.1)	42 (12.7)	

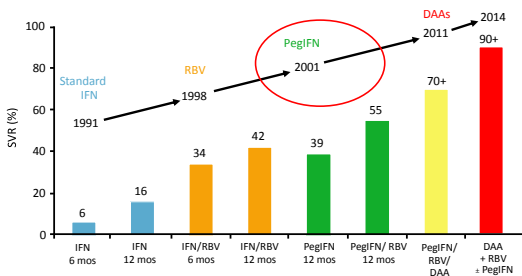
Avihingsanon et al. JGH 2014

Treatment challenges : High cost of HCV treatment in Asia

Countries	Anti HCV ab	HCV RNA USD	Peg IFN/RBV	Administrative costs	Total cost
China	\$5-\$10		\$18,000	Unknown	\$18,000
India	\$4-\$8	132	\$15,000-\$16,000	Unknown	\$15,000-\$16,000
Indonesia	\$25-\$	Few countries have a national plan to address/treat HCV Thailand			\$26,000-\$30,000
Nepal	\$2	HCV screening for general : No HCV screening in HIV: Yes National HCV treatment guideline: Yes			N/A
Thailand	\$6-\$9	100-120	\$18,000	\$15,000	\$33,000
Vietnam	\$10		\$12,000	\$16,000	\$28,000

Metheny, N. 2010. Dying for Treatment: HCV Treatment Out of Reach in Asia
Thai AIDS Treatment Action Group (TTAG)

Interferon free era



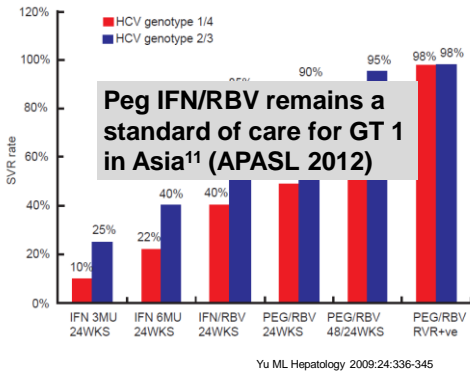
Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.

High SVR rates to Peg IFN/ribavirin combination therapy for chronic hepatitis C in Asia

Patient population	Treatment regimen	Country	SVR rate
Genotype 1:	PegIFN plus SD RBV for 48 weeks	China ¹	74%
		Japan ²	61%
		Korea ³	70%
		Taiwan ^{4,5,6}	76-79%
Genotype 1, LVL, and RVR	PegIFN plus SD RBV for 24 weeks	Taiwan ^{4,6}	94-96%
Genotype 2/3	PegIFN plus LD RBV for 24 weeks	China ¹	75%
		Taiwan ⁷	84%
		Korea ³	94%
Genotype 2/3 and RVR	PegIFN plus SD RBV for 24 weeks	Taiwan ⁸	95%
		Taiwan ⁸	100%
Genotype 4	PegIFN plus SD RBV for 48 weeks	Kuwait ⁹	68%
Genotype 6	PegIFN plus SD RBV for 48 weeks	Hong Kong ¹⁰	86%

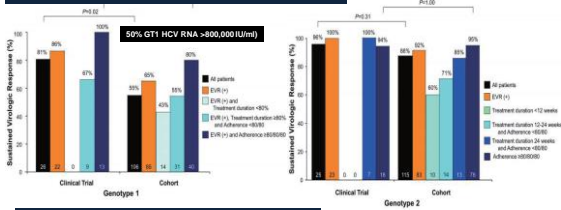
LD RBV, lower dose of ribavirin, 800 mg/day; LVL, low baseline viral loads; PegIFN, peginterferon; RVR, rapid virological response; SD RBV, standard dose of ribavirin, 1000-1200 mg/day; SVR, sustained virological response. ¹ Gastroenterol Hepatol 2007;22:858-61. ² Gastroenterol Hepatol 2007;22:855-62. ³ Korean J Hepatol 2008;14:46-51. ⁴ Clin Infect Dis 2008;47:1269-9. ⁵ Gastroenterology 2008;136:496-504. ⁶ Hepatology 2008;47:1884-93. ⁷ J Clin Gastroenterol 2008;42:1733-7. ⁸ J Infect Dis 2008;198:808-12. ⁹ APASL consensus statement Hepatol Int 2012;6:409.

High SVR rates in Asian HCV infection



Korea: High SVR rates in HCV GT1 with Peg/RBV in clinical practice

272 HCV¹
 Clinical trial group n=51 (GT1=26; cirrhosis 7.7% GT1)
 Clinical practice n=221 (GT1=106, cirrhosis 21.7% each)
 Peg alpha2a/RBV, 24 weeks for GT2



Non adherence (n=68: 25%)
 •lab abnormal :70% anemia, 35% neutropenia
 •Adverse symptoms: 54%

¹Heo NY CMH 2013;19:60-69

Factors contributing to SVR rates in HIV/HCV in Asia

- HIV-related immune suppression
 - Advanced HIV
- More advanced liver fibrosis¹
 - Insulin resistance^{2,3}
 - Genotype^{3†}
- Higher HCV RNA
- Higher treatment discontinuation
 - Toxicity : anemia, low body weight, mitochondrial toxicity
- Lower RBV dosing (800 mg vs 1000/1200 mg daily)
- Drug interaction

Favorable IL28B –CC
 Genotype 2/3

Peg IFN/RBV is a standard of care for GT 1 in Asia⁵ (APASL 2012)

⁵APASL consensus statement Hepatol Int 2012;6:409

¹Avhingsanon et al. JGH 2014 ² Patel et al. JGH 2011;26:1182 ³Hull et al. AIDS;26:1789 ⁴Barreiro P CID 2006; 42 :1032

HCV treatment in Japan

HCC 3rd leading cause of death in male, 4th in female
 50-76% of HCC due to HCV
 1.5-2 Million Japanese expected to have HCV infection

Approved DAAs:

- Simeprevir (Sep27,2013)
- Daclatasvir/asunaprevir (July7,2014)
- Sofosbuvir : submitted

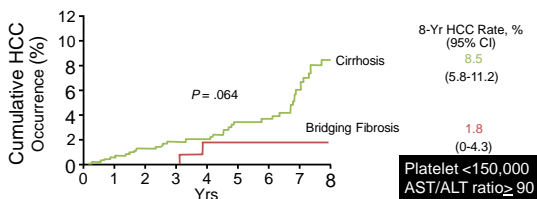
HCV treatment in HIV infected patients in developed countries is well established
But
 there is limited data in Asia and other RLS

Can we wait for new treatment?

Meta-analysis: Risk of HCC in HCV Pts With Advanced Fibrosis Following SVR

- 1000 patients with bridging fibrosis or cirrhosis who achieved SVR following IFN-based HCV therapy followed for median of 5.7 yrs
- Cirrhotics at greatest risk of HCC following SVR
- 51 cases developed HCC

Age >60 yrs : 12%(5.3-19.1)
 45-60 yrs:9.7(5.8-13.6)
 <45 yrs: 2.6%(0-5.5)



Van der Meer AJ, et al. AASLD 2013. Abstract 143. Reproduced with permission.

Effectiveness and Tolerability of Hepatitis C Treatment in HIV Co-infected Patients in Routine Care Services in Asia: A Pilot Model of Care Project

4 sites: Indonesia, Thailand, Vietnam, Malaysia.

Up to 400 HIV-infected patients under care (100 per site), and with known HCV Ab, will receive HCV-RNA testing.

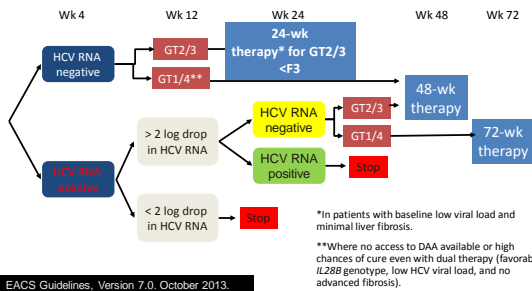
Those with confirmed chronic infection will receive:

- HCV genotyping
- IL28B testing,
- Liver fibrosis assessment with Fibroscan.

- 200 patients (50 per site) with treatment indication will be offered treatment with Pegylated-interferon and Ribavirin



Treatment with PegIFN/RBV Therapy in Coinfected Patients



EAACS Guidelines, Version 7.0, October 2013.

HCV RNA, genotype and IL28b

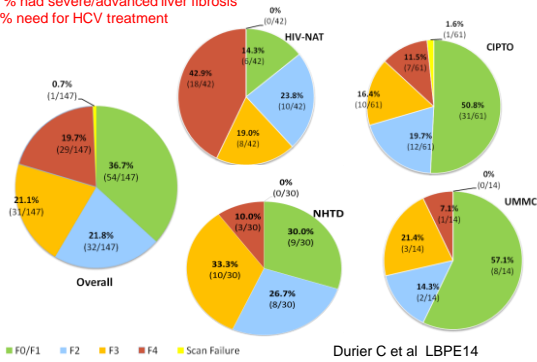
Male 87.9%, median age 38.6 years, IDU 75%, **heterosexual only 9.8%, MSM only 3.4%**, HBV co-infection 2.7%, alcohol 24.5%, CD4>350 68.3%, undetectable HIV RNA 86.7%

	Overall N=265	HIV-NAT,TH N=99	Cipto, IN N=86	NHTD, VN N=53	UMMC,MA N=27
Detectable HCV RNA, (%)	70.7	80.4	74.4	56.6	66.7
HCV RNA log10 Iu/ml, median (IQR)	6.28(4.67-6.63)	6.34(5.8-6.63)	6.24(5.68-6.59)	6.34 (5.72-6.56)	5.98(5.11-6.74)
HCV genotype,%					
1	59.4	40.6	78.6	60.0	28.6
1+others	6.6	6.3	2.4	12.0	14.3
3	19.8	43.8	7.1	0	57.1
4	1.9	0	4.8	0	0
6	10.3	10.1	0	4.0	0
Indeterminate, sequencing pending			7.1	24	0
IL28B CC	83.9	83.1	86.4	NA	NA

Durier C et al LBPE14

Liver fibrosis staging by fibroscan

40 % had severe/advanced liver fibrosis
63% need for HCV treatment



HCV treatment : preliminary result

	N=41
Male, N (%)	36 (87)
age, yrs	43 (37-48)
BW, kg	57 (51-70)
ALT, IU/L	77 (48-122)
Fibrosis score, Kpa	10.7 (8.4-17.5)
Fibrosis score >12.5KPa, N(%)	15 (37)
HCV RNAlog ₁₀ IU/ml	6.14 (5.5-6.58)
IL28B CC, N (%)	39 (95)
HCV genotype, %	
1a	24.4
1b	9.7
3	39
1a+others	7.3
6	19.5

Results

1 patient (GT3) had HCV RNA at week12 : <12 IU/ml

Genotype, N (%)	RVR	Week 4 declining > 2 log	Week 4 declining < 2 log
1a	2/10 (20%)	4/10 (40%)	4/10 (40%)
1b		3 / 4 (75%)	1 /4 (25%)
1+ other	2/3 (67%)		1/3 (23%)
3*	3/9 (33%)	5/9 (56%)	1 /9 (11%)
6**	1/7 (14%)	5/7 (71%)	1/7 (14%)

* Pending week4 HCV RNA =6 ** Pending week4 HCV RNA =1

90% week4 ALT improved and 41% : normal ALT at week 4

Weight loss 80%
Dose reduction 26.8%
BW: 4, Neutropenia (<750) /thrombocytopenia 5, anemia2

Thailand: Free HCV treatment (Peg IFN/RBV) for GT2/3

- Diagnostic and treatment monitoring costs are not covered.
- only 24 weeks of Peg IFN/RBV is provided (HIV-HCV requires 48 weeks)
- Reimbursement criteria are as follows:
 - o 18-65 years of age;
 - o HCV genotype 2&3 only;
 - o ALT $\geq 1.5 \times$;
 - o HCV RNA $\geq 5,000$ UI/ml;
 - o Liver biopsy metavir score ≥ 2 or fibroscan pKa ≥ 7.5 .
- o Funding coverage is needed for drugs, patient support, monitoring, and treatment complication

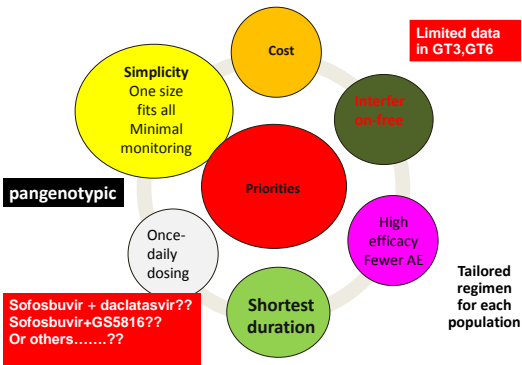
Thailand: Next step

- Free HCV treatment for all genotype, including co-infection
- National HIV treatment guideline 2014
 - HBsAg testing for all HIV
 - antiHCV testing for all HIV
 - annually HCV testing for active risk behavior (active PWID, MSM with multiple partners)
 - starting ARV at any CD4 cells counts
 - Consider HCV treatment
 - HCV RNA $\geq 5,000$ UI/ml;
 - on ART with HIV RNA < 50 copies/ml
 - HCC screening if cirrhosis

July 29, 2014 : Panel discussion

- to facilitate the process of new DAA approval
- affordable price of new DAAs
- New DAAs into National free program of HCV treatment

Future HCV Therapies in Asia and other resource limited settings



Summary

- awareness and education program on HCV treatment and care
- Facilitate integration of HCV-related services into routine HIV care settings
- Harm reduction strategies for PWID
- HCV screening in high risk population : PWID, MSM, sex worker, blood transfusion
- Regular HCV screening for HIV-infected MSM, PWID
- Improved access to ART and initiation ART earlier
- Enhanced liver disease staging (ie Fibroscan, Fib-4, APRI)
- Promote HCV treatment and care : treatment as prevention with **pangenotypes_IFN-free HCV treatment regimens**

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TREATASIA



Prof Joep Lange



"an extraordinary leader, scientist and humanitarian"
