Treating coinfection in Asia: Challenges and unmet needs

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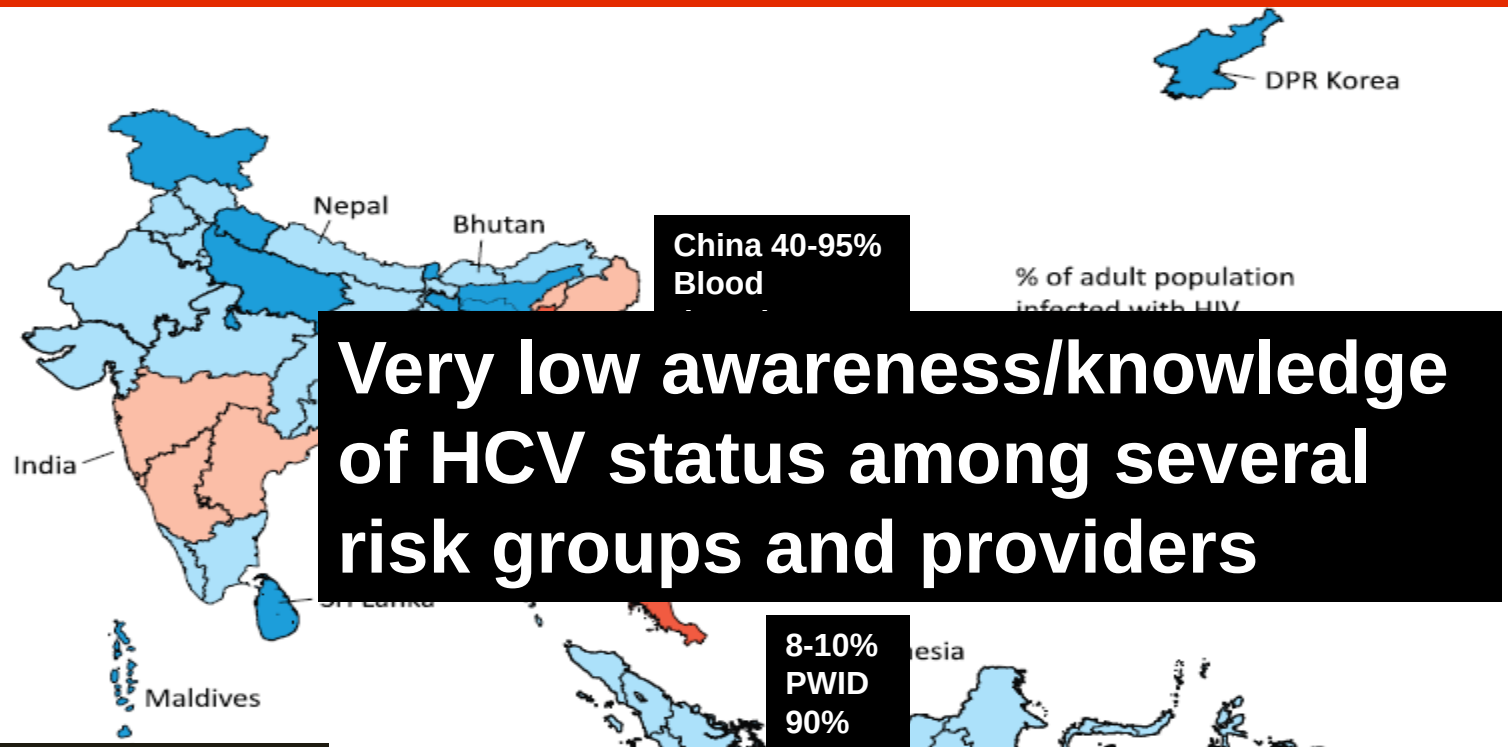
HIV/HCV coinfection: Public Health Challenges in Asia

- **prevalence, HCV genotype distribution and disease progression**
- **HCV treatment outcome in Asia**
- **Challenges in providing treatment and care**

Burden of HIV/HCV in Asia



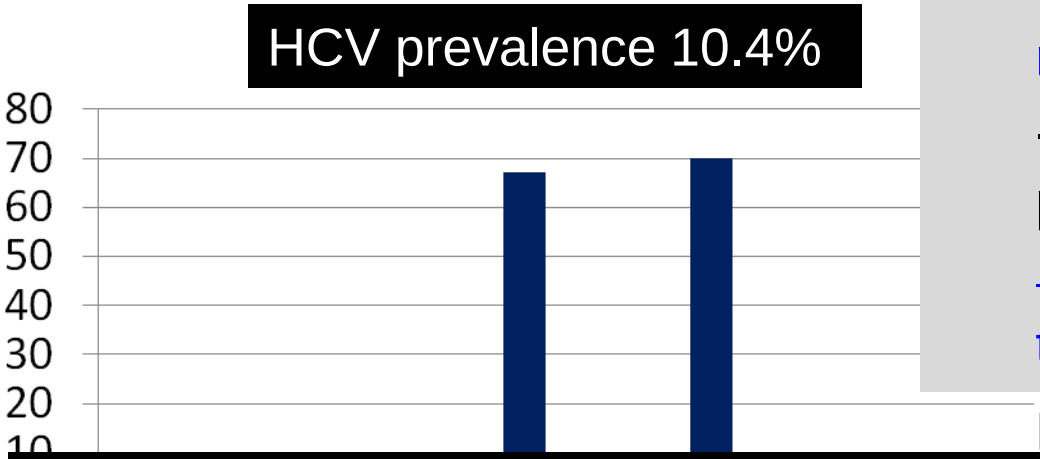
Very low awareness/knowledge of HCV status among several risk groups and providers

3.5 million HIV
32 million HCV

Prevalence of HIV/HCV co-infection has not been comprehensively estimated

HCV prevalence in Treat Asia HIV Database (N=1469) in 2005[1]

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



March 2012, N 6,360 in TAHOD:

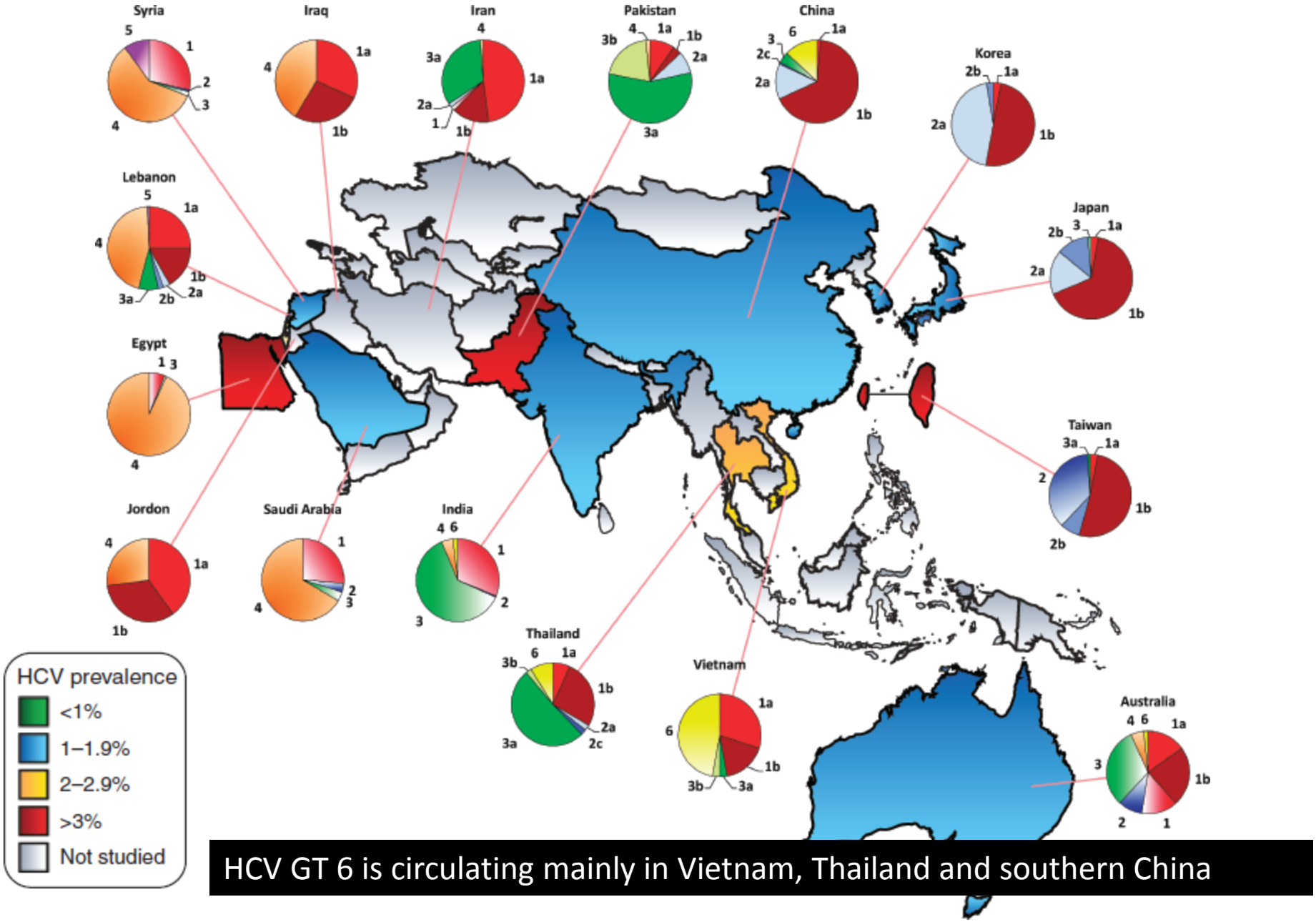
- –65.3% had HCV testing.
- −17.7% had positive HCV Ab.
- −Only 4.4% of those had received HCV PCR testing.
- −43.8% were found to have positive HCV RNA.
- –Only very few had received treatment.

Estimated 2-9 M PWID in Asia –

Underestimation of HCV coinfection and low number of PWID in HIV treatment and Care

Expensive, inadequate HCV RNA

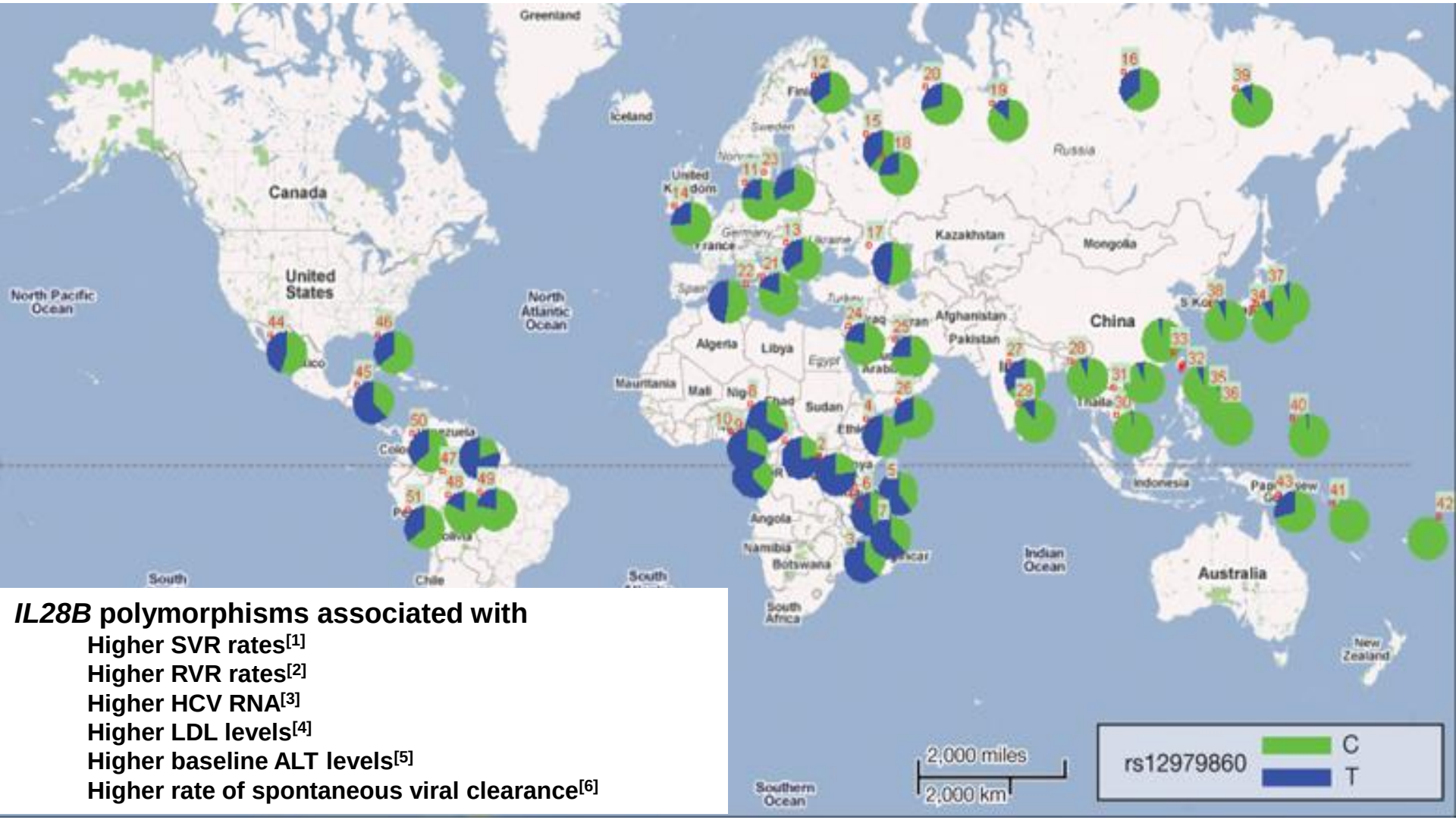
HCV incidence and genotype distribution in Asia



HCV GT 6 is circulating mainly in Vietnam, Thailand and southern China

Sievert et al. Liver International 2011:61-80

Favorable IL28B rs12979860 CC Genotype in Asia



***IL28B* polymorphisms associated with**

- **Higher SVR rates[1]**
- **Higher RVR rates[2]**
- **Higher HCV RNA[3]**
- **Higher LDL levels[4]**
- **Higher baseline ALT levels[5]**
- **Higher rate of spontaneous viral clearance[6]**

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 copies/ml				
FibroScan, PKa	10.5)	8.5 (6.4-13.85)	6.6 (4.9-9.5)	
<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)**	

2/3 meet criteria for treatment
1/4 require HCC screening

Multiple challenges of HIV/HCV management in Asia

Medical ineligibilities
Substance use
Psychiatric disorder
Co-morbidities :TB
Stage of liver disease

System barrier
Lack of access to care
Cost of drug and monitoring (HCV RNA, genotype, Liver biopsy/fibroscan)

Care provider barriers
Failure of screening
Lack of Rx knowledge
Social stigma

Patient barriers
Refusal
Adherence risk
Side effects, drug interaction
LTFU

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-$35**	**92**	**$17,000-$18,500**	**$9,000-$11,500**	**$26,000-$30,000**
Nepal	**$2**	**126**	**Treatment not available**	**N/A**	**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)

Lack of recognition of the importance of the drugs

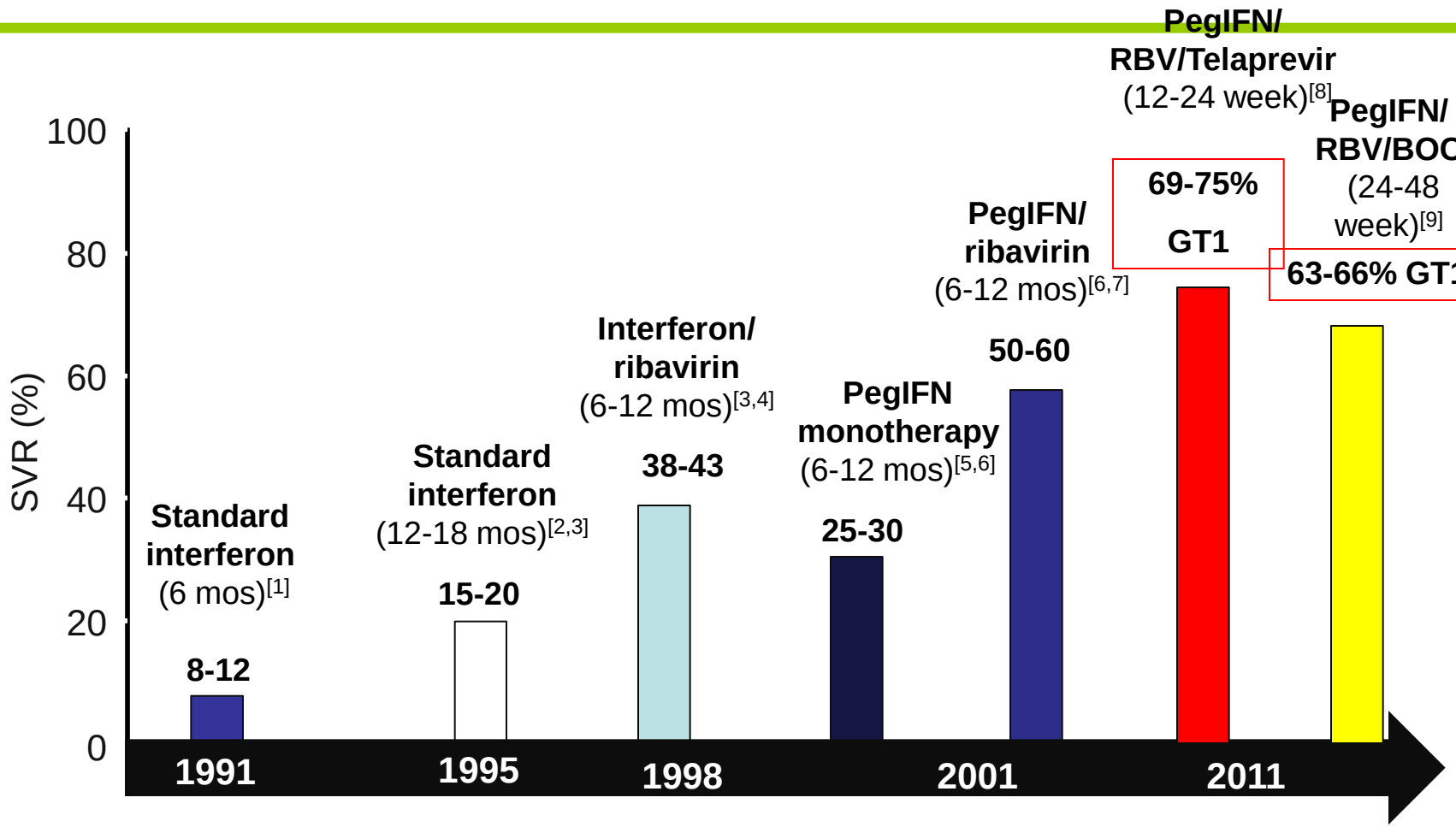
PEG-IFN and RBV not yet on the WHO Essential Medicines List

Marginal commitment from international donors to support efforts to tackle and treat Hep C.

Country Plans, Guidelines, and Resources

Few countries have a national plan to address/treat HCV

Treatment of Chronic Hepatitis C



1. Carithers RL Jr., et al. Hepatology. 1997;26(3 suppl 1):83S-88S. 2. Zeuzem S, et al. N Engl J Med. 2000;343:1666-1672. 3. Poynard T, et al. Lancet. 1998;352:1426-1432. 4. McHutchison JG, et al. N Engl J Med. 1998;339:1485-1492. 5. Lindsay KL, et al. Hepatology. 2001;34:395-403. 6. Fried MW, et al. N Engl J Med. 2002;347:975-982. 7. Manns MP, et al. Lancet. 2001;358:958-965. 8Jacobson IM, et al. N Engl J Med. 2011;364:2405-2416 9. Poordad F, et al. N Engl J Med. 2011;364:1195-1206

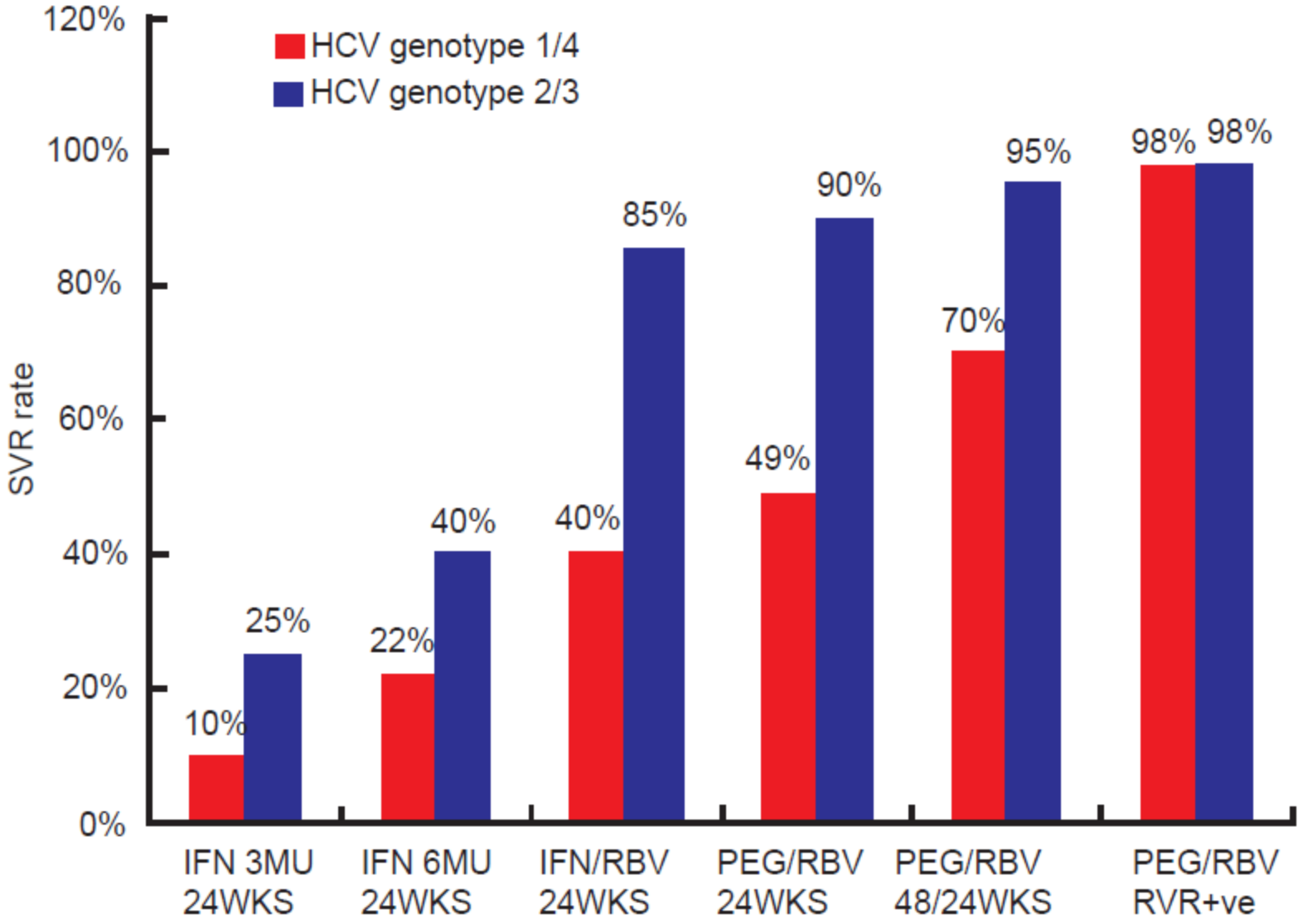
High SVR rates to Peg IFN/ribavirin combination therapy for chronic hepatitis C in Asia

Patient population	Treatment regimen	Country	SVR rate
Genotype 1:	PegIFN plus SD RBV for 48 weeks	China [1]	74%
		Japan [2]	61%
			70%
			76-79%
Genotype 1, LVL, and RVR			**94-96%**
Genotype 2/3	PegIFN plus LD RBV for 24 weeks	China	75%
		Taiwan [7]	84%
		Korea [3]	94%
	PegIFN plus SD RBV for 24 weeks	Taiwan [8]	95%
Genotype 2/3 and RVR	**PegIFN plus SD RBV for 16 weeks**	**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%

Peg IFN/RBV remains a standard of care for GT 1 in Asia[11]

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] J. Gastroenterol. Hepatol. 2007;22:832-6; [2] J. Gastroenterol. Hepatol. 2007;22:645-52; [3] Korean J. Hepatol. 2008;14:46-57; [4] Clin. Infect. Dis. 2008;47:1260-9; [5] Gastroenterology 2009;136:496-504; [6] Hepatology 2008;47:1884-93;[7] ??; [8] Gut 2007;56:553-9;[9] Am. J. Gastroenterol. 2004;99:1733-7; [10] J. Infect. Dis. 2008;198:808-12 [11]APASL consensus statement Hepatol Int 2012:6:409

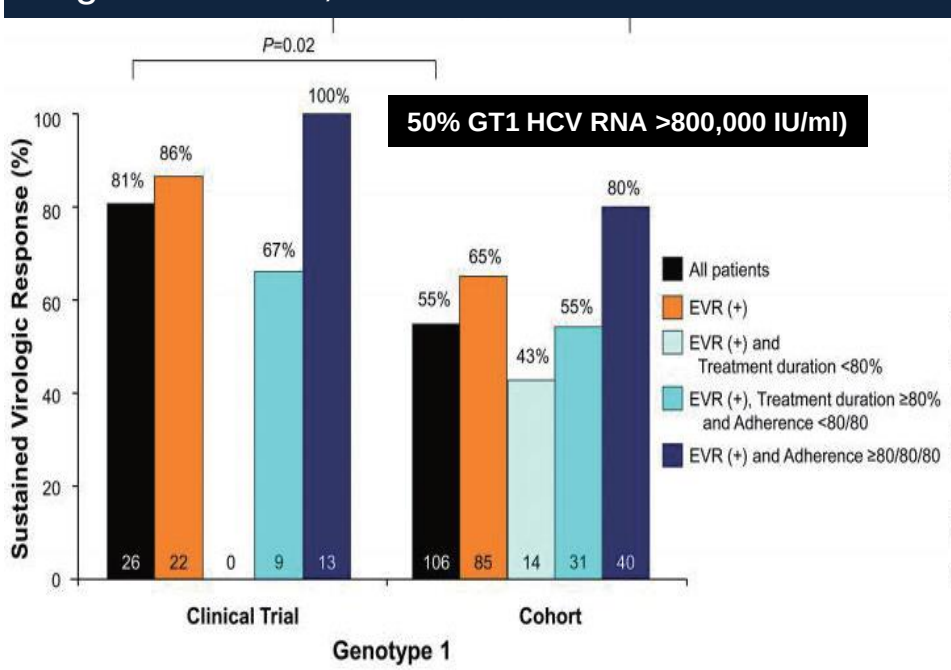
High SVR rates in Asian HCV infection

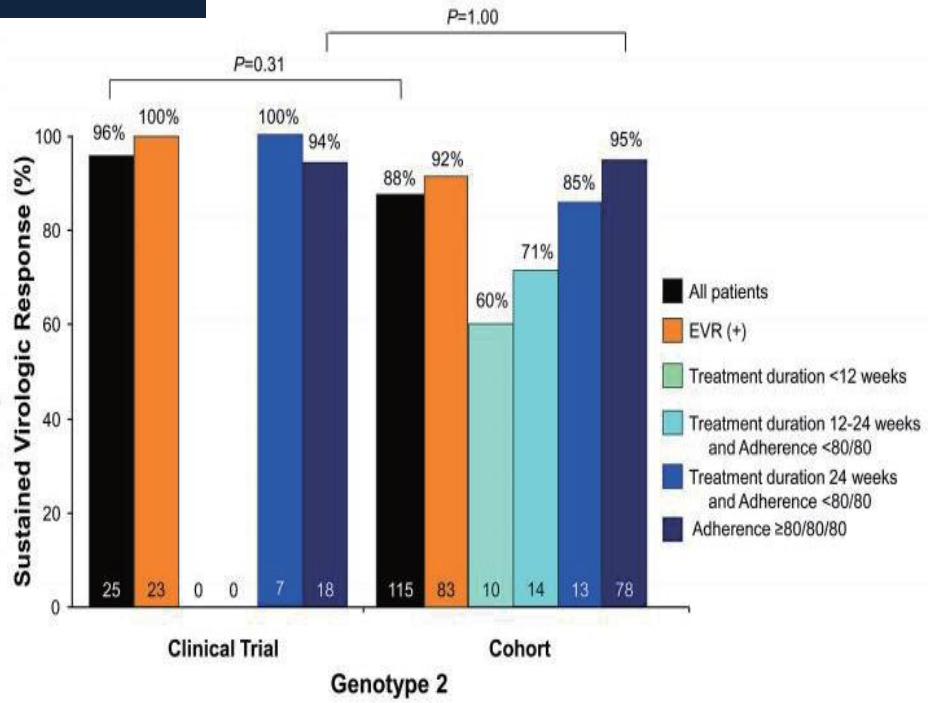


Yu ML Hepatology 2009:24:336-345

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

272 HCV[1]
Clinical trial group n=51(GT1=26; cirrhosis 7.7% GT1)
Clinical practice n=221 (GT1=106, cirrhosis 21.7% each)
Peg alfa2a/RBV, 24 weeks for GT2





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

[1]Heo 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 fibrosis[1]
  - Insulin resistance[2;3]
  - Genotype3[4]
- 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 Asia[5]

[5] APASL consensus statement Hepatol Int 2012:6:409

[1]Avihingsanon et al. APASL 2013 [2] Patel et al. JGH 2011:26:1182 [3]Hull et al. AIDS:26:1789 [4] Barreiro P CID 2006: 42 :1032

HCV treatment in HIV infected patients in developed countries is well established

But

there is limited data in Asia

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

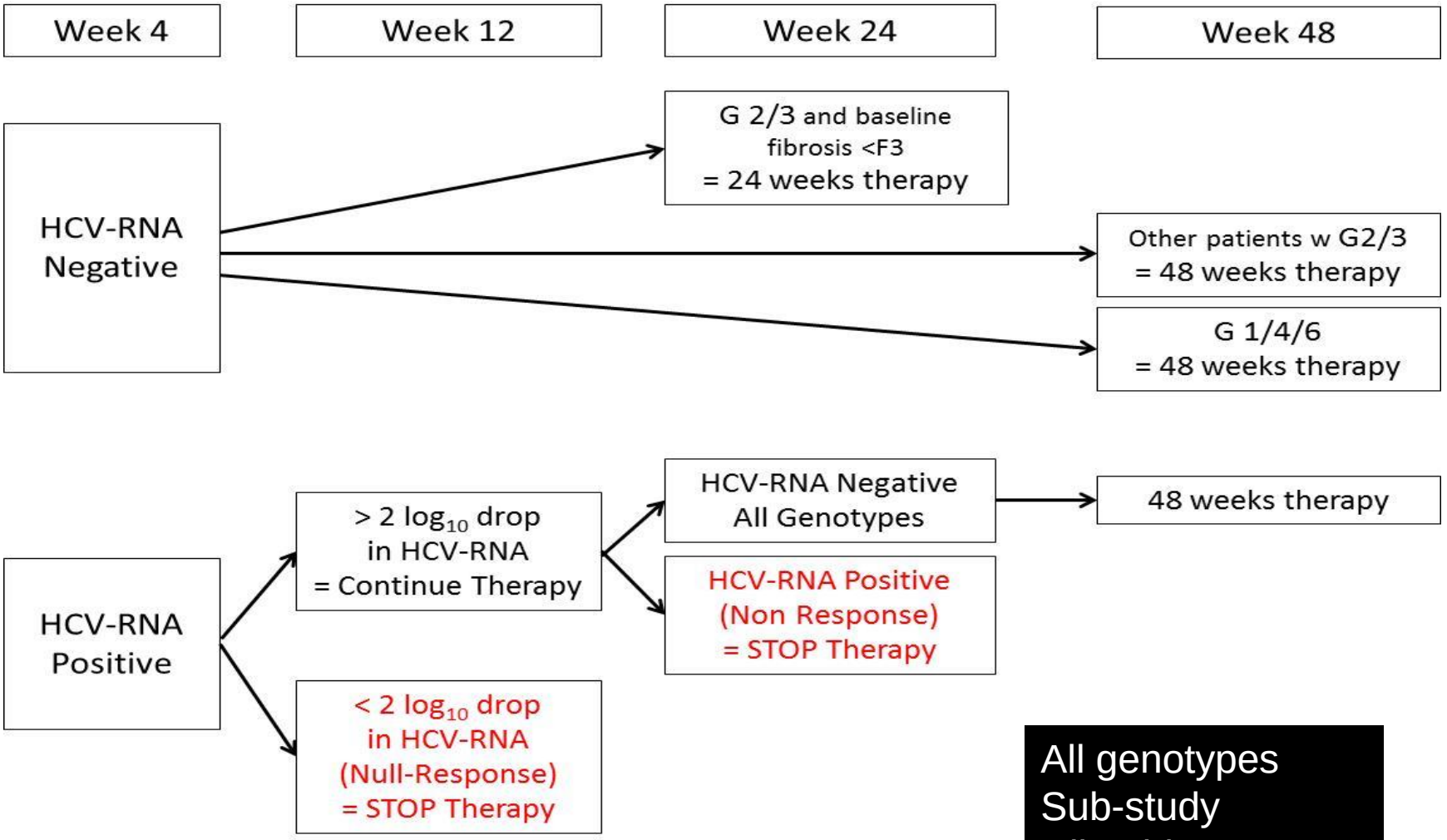
4 sites: Indonesia, Thailand, Vietnam, Malaysia.

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.

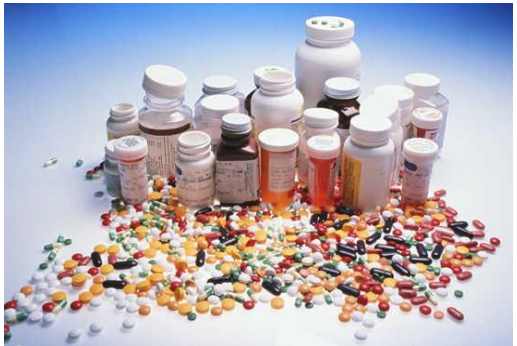
– 200 patients (50 per site) with treatment indication will be offered treatment with Pegylated-interferon and Ribavirin



All genotypes Sub-study Ribavirin PK (Thailand)

Challenges of Using Protease Inhibitors (Telaprevir:TPV; Boceprevir: BOC) in clinical practice

- Pill burden
  - BOC 4 X 200 mg 8 hourly = 12 capsules / day
  - TPV 2 X 375 mg 8 hourly = 6 tablets /day (9 if EFV)
- Need to have with food
  - TPV with 20g fat to increase absorption
  - BOC with food
  - Some HIV drugs have food restrictions (e.g. EFV needs to be taken in fasting state)
- Take with RBV (5-6 tablets/day)
- If HIV and on ART, further pill burden
- Potential issues of adherence
- Expensive
- Drug interaction with ARV and others (CYP450)
- Increase in adverse effects
  - TPV: anemia, rash
  - BOC: anemia, dysguesia
- Concerns over resistance



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 ≥ 1.5 x;
    - o HCV RNA ≥ 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

Countries	*Population*	*HCV estimates*	*Cases treated*
Taiwan	23 M	490,000	9,000
Thailand	67 M	1,200,000	3,000
Malaysia	30 M	30,000	1,000
Vietnam	90 M	1,800,000	1,500
Myanmar	49 M	1,000,000	500
India	1100 M	10,000,000	8,000

Source : MSD

Conclusion: strategies to reduce disease burden of HIV/HCV coinfection in Asia

- awareness and education program on HCV
- 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)
- Promote HCV treatment and care : treatment as prevention
- **IFN-free HCV treatment regimens**

TEST

New Infection, death, discrimination

Getting to zero

HCV is curable

TREAT

It is absolutely impossible to put a price on the patient's quality of life as it is priceless and invaluable

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