Role of IFN-based therapy for HCV in the Asian region

WEI Lai
Peking University People's Hospital
Peking University Hepatology Institute

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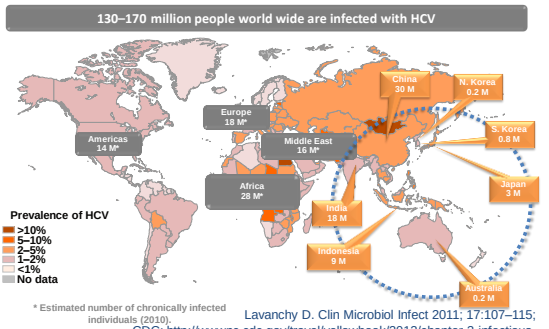
- Epidemiology and disease burden of HCV infection in Asia
- IFN and Ribavirin for Chronic Hepatitis C in Asia
- Standard of Care in Asia currently
- IFN-based triple therapy in Asian GT-1 patients
- IFN-free in Asia in near future

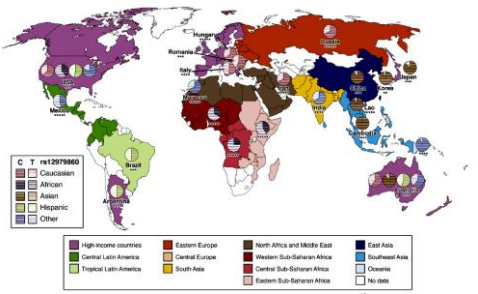
Epidemiology and disease burden of HCV infection in Asia

HCV distribution across the world heavy disease burden in AP



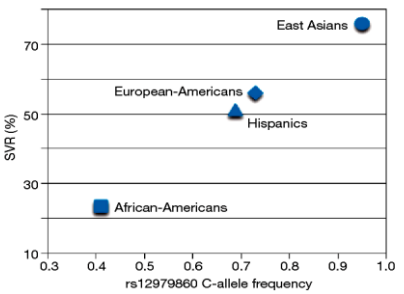
Lavanchy D. Clin Microbiol Infect 2011; 17:107–115;
CDC: http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/hepatitis-c.htm.

Distribution of IL-28B genotype



Wei L, Lok AS. Gastroenterology. 2014;146(5):1145-1150

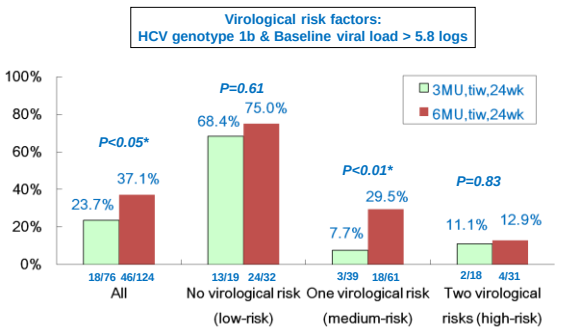
Rate of SVR and rs12979860 C-Allele Frequency in Diverse Ethnic Groups



Ge et al. Nature 2009; 461: 399-401

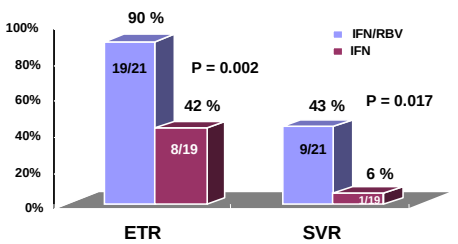
IFN and Ribavirin for Chronic Hepatitis C in Asia

3MU vs. 6 MU of IFN-α tiw for 24 Weeks in CHC



Yu ML, et al. BMC Infect Dis 2005; 5: 27

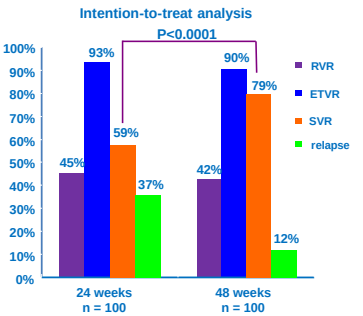
ETR and SVR to 24-week IFN/Ribavirin Combination Therapy and IFN Monotherapy in CHC Patients



Lai et al. Gastroenterology 1996; 111: 1307-1312.

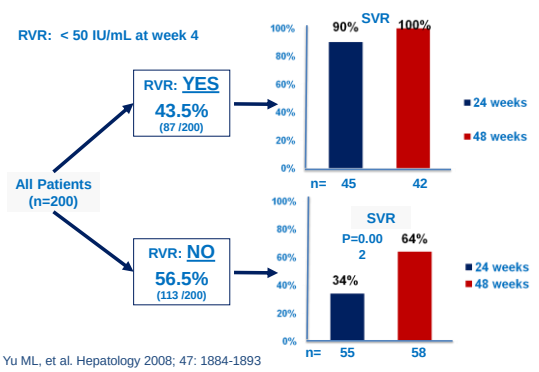
Standard of Care in Asia currently

Higher SVR with 48wk than 24 weeks PegIFN/RBV for HCV-1



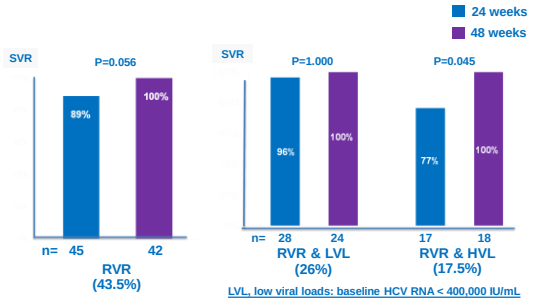
Yu ML, et al. Hepatology 2008; 47: 1884-1893

RVR Predicting Higher SVR in Genotype-1 Patients



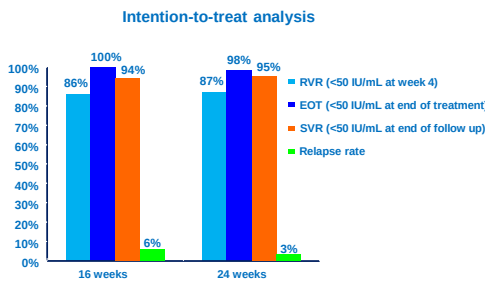
Yu ML, et al. Hepatology 2008; 47: 1884-1893

Baseline LVL with RVR Had an high SVR even in 24-wk Treatment



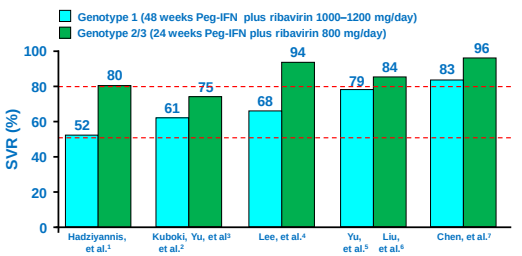
Yu ML, et al. Hepatology 2008; 47: 1884-1893.

Simialr SVR between 16 and 24-Wk in GT-2



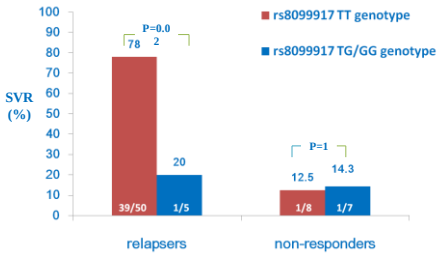
Yu ML, et al, Gut 2007; 56: 553-559.

Asian populations respond relatively well to current dual therapy compared with Caucasians



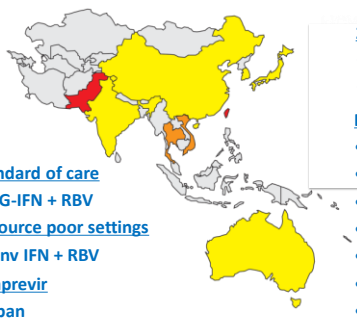
1. Hadziyannis SJ, et al. Ann Intern Med 2004; 140: 346; 2. Kuboki M, et al. J Gastroenterol Hepatol 2007; 22: 645
3. Yu JW, et al. J Gastroenterol Hepatol 2007; 22: 832; 4. Lee HJ, et al. Korean J Hepatol 2008; 14: 46
5. Yu ML, et al. Hepatology 2008; 47: 1884; 6. Liu CJ, et al. Gastroenterology 2009; 136: 496
7. Chen W, et al. Chin J Hepatol 2010; 18: 585

HCV-1 Treatment Experienced Patients Retreated by Peg-IFN and RBV for 48 Weeks
-Stratified by IL-28B Genotype



Huang CF, et al. J Gastroenterol Hepatol 2013; 28: 1515-1520

HCV treatments in Asia



Standard of care
- PEG-IFN + RBV

Resource poor settings
- Conv IFN + RBV

Telaprevir
- Japan
- Australia

2nd Gen DAA
- Simeprevir (Japan)
- DCV + ACV (Japan)

Boceprevir
- Singapore
- Malaysia
- Hong Kong
- Indonesia
- Philippines
- Vietnam
- Australasia

APASL 2012 Consensus Statements
Treatment of HCV Infection

12. In chronic HCV genotype 1 infection, the following apply:

- Treatment with peginterferon and ribavirin for 48 weeks is recommended.
- In patients who achieve an RVR at week 4, treatment can be discontinued after 24 weeks if the HCV RNA at baseline is < 400,000 IU/mL.
- In patients who achieve a complete EVR at week 12, treatment should be continued up to 48 weeks.
- In patients who do not achieve an EVR at week 12, but show a significant reduction in HCV RNA levels (partial EVR) and negativity of HCV RNA at week 24 (late virological response, LVR), treatment may be continued up to 72 weeks.

Omata et al. Hepatol Int 2012; 6: 409

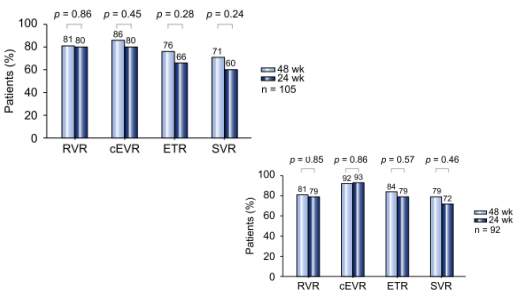
APASL 2012 Consensus Statements
Treatment of HCV Infection

13. In chronic HCV genotype 2/3 infection, the following apply

- Treatment with either conventional interferon alfa plus ribavirin or peginterferon alfa with or without ribavirin for 24 weeks is recommended (although peginterferon plus ribavirin might be more effective in patients with cirrhosis or a high viral load).
- There is some evidence that shortening duration of therapy to 16 weeks in patients with HCV genotype 2 infection provides equal SVR to 24 weeks of treatment.

Omata et al. Hepatol Int 2012; 6: 409

High SVR in GT6 by Peg-IFN and RBV with both 24 weeks and 48 weeks



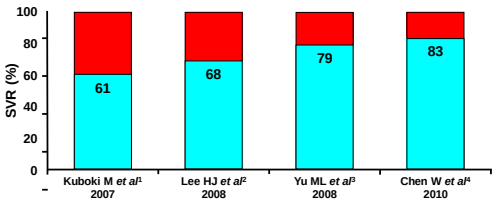
Thu Thuy PT, et al. Journal of Hepatology 2012,56,1012–1018

IFN-based triple therapy in Asian GT-1 patients

Despite achieving high SVR rates, there is still room for improvement in Asian patients

Genotype (GT) 1

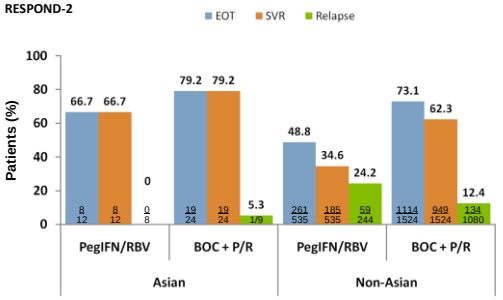
48 weeks Peg-IFN α-2a 180 µg/week plus ribavirin 1000–1200 mg/day



1. Kuboki M, et al. J Gastroenterol Hepatol 2007; 22: 645
2. Lee HJ, et al. Korean J Hepatol 2008; 14: 46
3. Yu ML, et al. Hepatology 2008; 47: 1884
4. Chen W, et al. Chin J Hepatol 2010; 18: 585

SVR rates with BOC + PegIFN/RBV in Asian vs non-Asian patients

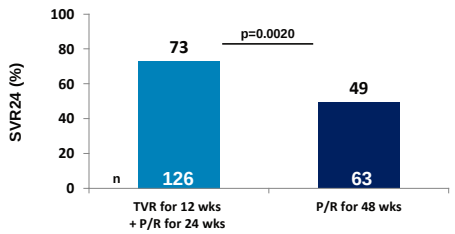
SPRINT-1/2
RESPOND-2



Hu KQ, et al. Hepatol Int 2012; 6:164.

SVR rates with TVR + PegIFN alfa/RBV in Japanese treatment-naive patients

G1 treatment-naive Japanese patients



Telaprevir + PegIFN alfa-2b + Ribavirin.

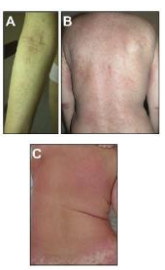
Kumada H, et al. J Hepatol 2012; 56:78–84.

Anaemia in triple therapy trials

Patients, %	Boceprevir[1,2]	Telaprevir[3]
Dose reduction RBV	19–22	22
EPO	41–46	No
Transfusions	–	Rare (1.6)
Discontinuation	0–3	TVR alone: 3 All drugs: 0.9

1. Poordad F, et al. Hepatology 2010; 52(Suppl.): 402A
2. Bacon BR, et al. Hepatology 2010; 52(Suppl.): 430A
3. Data on file: TVR/DoF/January2011/EMEA01

Telaprevir skin rash



Grade 1/mild (image A)
- Do not stop telaprevir
- Treat with topical steroids, antihistamines, emollients

Grade 2/moderate (image B)
- Do not stop telaprevir
- Treat with topical steroids, antihistamines, emollients

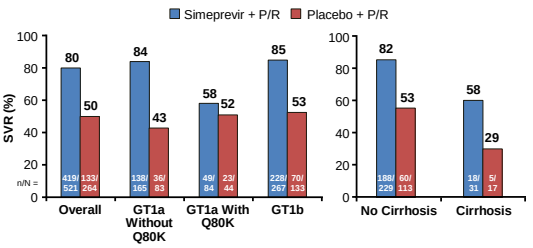
Grade 3/severe (no image shown)
- Stop telaprevir immediately
- Treat with topical steroids, antihistamines, emollients

Grade 4/life-threatening or systemic reactions (image C)
- Stop all treatment permanently
- Treat with systemic corticosteroids

Cacoub P, et al. J Hepatol. 2012; 56: 455-463.

Efficacy With Simeprevir + P/R in Tx-Naive GT1 Patients: Phase III Trials

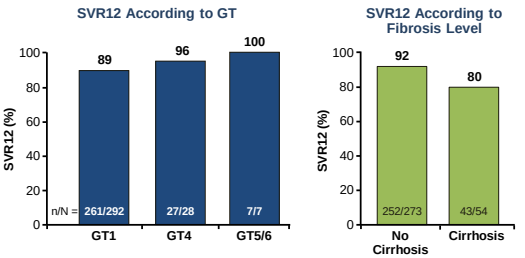
- SMV + P/R for 12 wks followed by 12-36 wks of P/R (placebo control)



Simeprevir prescribing information. Jacobson I, et al. EASL 2013. Abstract 1425.

Efficacy With Sofosbuvir + P/R in Tx-Naive GT1/4/5/6 Patients: Phase III Trials

- Single-arm study of sofosbuvir + P/R for 12 wks



Lawitz E, et al. N Engl J Med. 2013;368:1878-1887.

Treatment of GT-1 patients by IFN-based triple therapy in Asia

What we can do

Population	Disease	Regimens	Benifits
General GT1 Cirrhosis Relapses null response	Advanced liver disease Affordable or reimbursed	Now: BOC/P/R or TVR/P/R Near future: SIM/P/R, or SOF/P/R	increase SVR Shorten duration

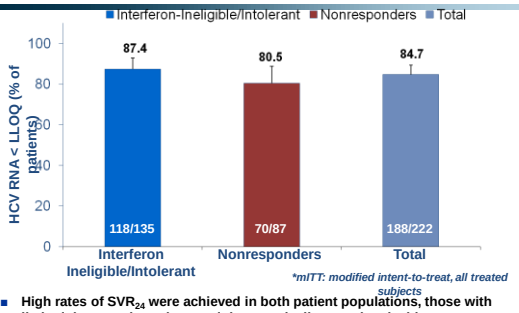
Treatment of GT-1 patients by IFN-based triple therapy in Asia

What we can NOT do and should do

Population	Regimens
IFN or RBV ineligible IFN or RBV intolerable Co-morbidities	IFN-free

IFN-free in Asia in near future

DCV+ASV in GT1b with IFN intolerant and ineligible



- **High rates of SVR_{24} were achieved in both patient populations, those with limited therapeutic options and those typically associated with poor responses to other therapies**

Chayama K, et al.AASLD 2013

New DAAs and new regimens

Trials	cirrhosis	SVR	regimens	Duration(wks)
SAPPHIRE-I	Yes	96.2%	ABT-450 + ombitasvir + Dasabuvir + RBV	12
ION-3	No	94%	LDV + SOF	8
		93%	LDV+ SOF + RBV	8
		95%	LDV+ SOF	12
ION-1	16%	99%	LDV+ SOF	12
		97%	LDV+ SOF + RBV	24
		98%	LDV+ SOF	12
		99%	LDV+ SOF + RBV	24
SAPPHIRE-II	No	96.3%	ABT-450 + ombitasvir + Dasabuvir+ RBV	12
ION-2	20%	94%	LDV+ SOF	12
		96%	LDV+ SOF + RBV	12
		99%	LDV+ SOF	24
		99%	LDV+ SOF + RBV	24
TURQUOISE-II	yes	91.8%	ABT-450 + ombitasvir +	12
		95.9%	Dasabuvir + RBV	24

* TN *TE * TN and TE

EASL 2014

Potential population to be treated with IFN-free in near future in Asia

- Not responding to Peg-IFN/RBV
  - Null response
  - Relapses
- IFN intolerant
  - Adverse effects
- Ineligible for Peg-IFN/RBV
  - Low ANC, BPC
  - Co morbidities

Summary

- Combination therapy with pegIFN and ribavirin is still the SOC for treatment of CHC in most of Asian countries.
- Baseline virological factors, on treatment viral kinetics, and the host factors may help making decision to treat chronic hepatitis C with pegIFN and ribavirin.
- IL28B polymorphisms before treatment is helpful while
- treating genotype 1 CHC with pegIFN and ribavirin.
- Combination therapy with DAA and SOC can increase the SVR rates both in naïve patients and treatment-experienced patients. IFN-free regimens will be the SOC in the near future.
- IFN-free regimens will be the SOC in near future, particularly in IFN ineligible and intolerant

Thanks !