Current Practice of HCV Treatment in China

Jidong Jia, MD, PhD

Liver Disease Research Center,
Beijing Friendship Hospital
Capital Medical University
Anti-HCV Prevalence in Different Age Groups in 1992 and 2006

Number of newly diagnosed HCV infection in mainland China reported to the CDC

China CDC report

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of HCV-infected patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>2114</td>
</tr>
<tr>
<td>2004</td>
<td>39380</td>
</tr>
<tr>
<td>2005</td>
<td>52927</td>
</tr>
<tr>
<td>2006</td>
<td>70681</td>
</tr>
<tr>
<td>2007</td>
<td>92378</td>
</tr>
<tr>
<td>2008</td>
<td>108446</td>
</tr>
<tr>
<td>2009</td>
<td>130575</td>
</tr>
<tr>
<td>2010</td>
<td>153039</td>
</tr>
<tr>
<td>2011</td>
<td>173872</td>
</tr>
</tbody>
</table>
Distribution of HCV genotype in China

HCV Genotype
- 1b
- 1a
- 2b
- 2a or 2c
- 3b
- 3a
- 6c
- 6a or 6b
- Multiple genotypes
- Unidentifiable

IL 28 B Distribution in China

How Many CHC Patients Received Antiviral Treatment in China?

<table>
<thead>
<tr>
<th>Region</th>
<th>Undiagnosed</th>
<th>Diagnosed but not TX</th>
<th>TX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worldwide</td>
<td>70%</td>
<td>79.6%</td>
<td>84.6%</td>
</tr>
<tr>
<td>US</td>
<td>27%</td>
<td>16.7%</td>
<td>13.5%</td>
</tr>
<tr>
<td>EU</td>
<td>1.9%</td>
<td>4.6%</td>
<td>16.3%</td>
</tr>
<tr>
<td>Japan</td>
<td>12%</td>
<td>18%</td>
<td>79.1%</td>
</tr>
<tr>
<td>China</td>
<td>10%</td>
<td>5.5%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Slide courtesy of Prof. ZHUANG Hui
PEG IFN/R (even IFN/RIB) is still the current SOC in China

Genotype 1

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

<table>
<thead>
<tr>
<th>SVR (%)</th>
<th>Caucasian</th>
<th>Asian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hadziyannis SJ et al. 2004</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Kuboki M et al. 2007</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Lee HJ et al. 2008</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Yu ML et al. 2008</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Chen W et al. 2010</td>
<td>83</td>
<td></td>
</tr>
</tbody>
</table>

## DAAs Registration Status in Mainland China

<table>
<thead>
<tr>
<th>company</th>
<th>DAAs</th>
<th>Protocol</th>
<th>China Registration status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CTA</td>
</tr>
<tr>
<td>J&amp;J</td>
<td>Simeprevir</td>
<td>Simeprevir+PegIFNα/RBV</td>
<td>2011/01/28</td>
</tr>
<tr>
<td>BMS</td>
<td>Daclatasvir +Asunaprevir</td>
<td>Daclatasvir+Asunaprevir</td>
<td>2012/11/01</td>
</tr>
<tr>
<td>Gilead</td>
<td>Sofosbuvir</td>
<td>Sofosbuvir+RBV ± PegIFN</td>
<td>2013/08</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/Ledipasvir (FDC)</td>
<td>Sofosbuvir/Ledipasvir (FDC) ± RBV</td>
<td>Wave 2</td>
</tr>
<tr>
<td>AbbVie</td>
<td>3D</td>
<td>3D+RBV</td>
<td>2014/04</td>
</tr>
<tr>
<td>MSD</td>
<td>MK5172 MK8742</td>
<td>MK5172 MK8742 ± RBV</td>
<td></td>
</tr>
</tbody>
</table>
Hepatitis C drugs not reaching poor

Treatment guidelines for virus highlight challenge of paying for expensive drugs in low-income countries.

Ewen Callaway
CHRONIC HEPATITIS C TREATMENT EXPANSION
Generic Manufacturing for Developing Countries

Gilead is committed to increasing access to its medicines for all people who can benefit from them, regardless of where they live or their ability to pay.

The licensing agreement encompasses the following countries:

<table>
<thead>
<tr>
<th>Afghanistan</th>
<th>Chad</th>
<th>Guatemala</th>
<th>Maldives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>Comoros</td>
<td>Guinea</td>
<td>Mali</td>
</tr>
<tr>
<td>Antigua and Barbuda</td>
<td>Congo, DR</td>
<td>Guinea-Bissau</td>
<td>Mauritania</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>Congo, Rep.</td>
<td>Guyana</td>
<td>Mauritius</td>
</tr>
<tr>
<td>Benin</td>
<td>Cote d’Ivoire</td>
<td>Haiti</td>
<td>Mongolia</td>
</tr>
<tr>
<td>Bhutan</td>
<td>Cuba</td>
<td>Honduras</td>
<td>Mozambique</td>
</tr>
<tr>
<td>Bolivia</td>
<td>Djibouti</td>
<td>India</td>
<td>Myanmar</td>
</tr>
<tr>
<td>Botswana</td>
<td>Dominica</td>
<td>Indonesia</td>
<td>Namibia</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>Egypt</td>
<td>Kenya</td>
<td>Nauru</td>
</tr>
<tr>
<td>Burundi</td>
<td>Equatorial Guinea</td>
<td>Kiribati</td>
<td>Nepal</td>
</tr>
<tr>
<td>Cambodia</td>
<td>Eritrea</td>
<td>Kyrgyz Republic</td>
<td>Nicaragua</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Ethiopia</td>
<td>Lao PDR</td>
<td>Niger</td>
</tr>
<tr>
<td>Cape Verde</td>
<td>Fiji</td>
<td>Lesotho</td>
<td>Nigeria</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>Gabon</td>
<td>Liberia</td>
<td>North Korea</td>
</tr>
<tr>
<td>Ghana</td>
<td>Gambia</td>
<td>Madagascar</td>
<td>Pakistan</td>
</tr>
<tr>
<td></td>
<td>Ghana</td>
<td>Malawi</td>
<td>Palau</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td>Rwanda</td>
<td>Samoa</td>
<td>Senegal</td>
</tr>
<tr>
<td></td>
<td>Sao Tome &amp; Pr.</td>
<td>Seychelles</td>
<td>Sierra Leone</td>
</tr>
<tr>
<td></td>
<td>Senegal</td>
<td>Solomon Islands</td>
<td>Somalia</td>
</tr>
<tr>
<td>South Africa</td>
<td>South Sudan</td>
<td>St. Vincent and the Grenadines</td>
<td>Swaziland</td>
</tr>
<tr>
<td></td>
<td>Sri Lanka</td>
<td>Tanzania</td>
<td>Tajikistan</td>
</tr>
<tr>
<td></td>
<td>Sudan</td>
<td>Timor Leste</td>
<td>Togo</td>
</tr>
<tr>
<td></td>
<td>Suriname</td>
<td>Tonga</td>
<td>Togo Leste</td>
</tr>
<tr>
<td></td>
<td>Uganda</td>
<td>Turkmenistan</td>
<td>Tuvalu</td>
</tr>
<tr>
<td></td>
<td>Uzbekistan</td>
<td>Vanuatu</td>
<td>Vietnam</td>
</tr>
<tr>
<td></td>
<td>Vanuatu</td>
<td>Zambia</td>
<td>Zimbabwe</td>
</tr>
</tbody>
</table>

*The way of patients: Purchase DAAs from India!*

[www.gilead.com](http://www.gilead.com)
A higher uptake of IFN-free regimens will lead to increased virologic cure rates

<table>
<thead>
<tr>
<th></th>
<th>Old PegIFN/RBV therapy</th>
<th>90% SVR rates</th>
<th>90% SVR rates and higher treatment uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HCV patients</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Treatment uptake</td>
<td>10%</td>
<td>10%</td>
<td>90%</td>
</tr>
<tr>
<td>Cure</td>
<td>5%</td>
<td>9%</td>
<td>81%</td>
</tr>
</tbody>
</table>

Courtesy of Markus Cornberg, Hannover.
Current Practices in Asia: India

DR. SAMIR R. SHAH

Head, Dept of Hepatology
Institute of Liver Diseases, HPB Surgery and Transplant
Global Hospitals, Mumbai, India
Visiting Consultant, Jaslok and Breach Candy Hospital

Founder Trustee and Hon. Gen. Secretary
National Liver Foundation

Founder Executive Committee Member, CEVHAP
## EPIDEMIOLOGY OF HEPATITIS C VIRUS IN INDIA

<table>
<thead>
<tr>
<th>Authors</th>
<th>Geographic location</th>
<th>N</th>
<th>% Anti HCV Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population Studies</td>
<td>9 villages in Birbhum dist of WB</td>
<td>3579</td>
<td>0.87%</td>
</tr>
<tr>
<td>Chowdhary et al</td>
<td>Punjab</td>
<td>5258</td>
<td>5.2%</td>
</tr>
<tr>
<td>Sood et al</td>
<td>Haryana</td>
<td>7114</td>
<td>21%</td>
</tr>
<tr>
<td>Sachdev etal</td>
<td>Indian Armed Force</td>
<td>22666</td>
<td>0.44%</td>
</tr>
<tr>
<td>Singh et al</td>
<td>Maharashtra</td>
<td>1054</td>
<td>0.09%</td>
</tr>
<tr>
<td>Chadha etal</td>
<td>Puducherry</td>
<td>978</td>
<td>0.2%</td>
</tr>
<tr>
<td>Oli etal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Studies in Tribal Population</td>
<td>Arunachal Pradesh Lisu Com. Andhra Pradesh Baigas, Baharias, Saharias in MP and Chhatisgarh</td>
<td>380</td>
<td>2.02%</td>
</tr>
<tr>
<td>Phukan Ac et al, Chandra M et al, Rao VG et al</td>
<td></td>
<td>526</td>
<td>1.0% - 14.4%</td>
</tr>
<tr>
<td>Blood Bank Data</td>
<td>Northern States</td>
<td></td>
<td>0.29% - 1.85%</td>
</tr>
<tr>
<td></td>
<td>Southern States</td>
<td></td>
<td>0.27% - 1.17%</td>
</tr>
<tr>
<td></td>
<td>Eastern States</td>
<td></td>
<td>0.31% - 1.09%</td>
</tr>
<tr>
<td></td>
<td>Western States</td>
<td></td>
<td>0.0 - 0.9%</td>
</tr>
<tr>
<td></td>
<td>Armed Forced Blood Bank</td>
<td>39646</td>
<td>0.51%</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>South India, Delhi, North India</td>
<td></td>
<td>0.6% - 1.4%</td>
</tr>
<tr>
<td>Pratibhan R et al, Kumar A et al, Sood A et al</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Overall and Regional HCV Genotype Distribution

- North (5 sites)
  - GT 1 (n=120)
  - GT 3 (n=272)
  - GT 4 (n=29)
  - GT 5 (n=1)
  - Indeterminate (n=62)
  - Missing (n=16)

- East (5 sites)
  - GT 1 (n=120)
  - GT 3 (n=272)
  - GT 4 (n=29)
  - GT 5 (n=1)
  - Indeterminate (n=62)
  - Missing (n=16)

- South (4 sites)
  - GT 1 (n=120)
  - GT 3 (n=272)
  - GT 4 (n=29)
  - GT 5 (n=1)
  - Indeterminate (n=62)
  - Missing (n=16)

- West (5 sites)
  - GT 1 (n=120)
  - GT 3 (n=272)
  - GT 4 (n=29)
  - GT 5 (n=1)
  - Indeterminate (n=62)
  - Missing (n=16)

Overall:
- GT 1 (3%)
- GT 3 (12%)
- GT 4 (6%)
- GT 5 (24%)
- <1%
- Indeterminate (54%)
- Missing (6%)

Genotype was assayed using LINEAR ARRAY Hepatitis C Virus Genotyping Test for use with AMPLICOR® and COBAS®-AMPLICOR HCV Test, v2.0.
Access To New DAAs in Rx of HCV

- Availability
- Accessibility
- Affordability
- Acceptability

Sofosbuvir licensed for use in the India

Generic Sofosbuvir and Sovaldi
Both available at 11 USD/day
<table>
<thead>
<tr>
<th>Item</th>
<th>Cost (In USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sovaldi/day</td>
<td>11.10</td>
</tr>
<tr>
<td>Generic Sofosbuvir</td>
<td>6.73</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>0-0.45</td>
</tr>
<tr>
<td>Diagnostic Subsidized</td>
<td></td>
</tr>
<tr>
<td>HCVRNA Quantitative (Pre treatment, Week 4, Week 12, Week 24, and SVR 12/24)</td>
<td>0-196.35</td>
</tr>
<tr>
<td>CBC/LFT/PT/INR/Electrolytes/Creatinine</td>
<td>15.22</td>
</tr>
<tr>
<td>Cost for 24 weeks Sofosbuvir + Ribavirin with diagnostics</td>
<td>2526.48</td>
</tr>
</tbody>
</table>
Access To New DAAs in Rx of HCV

- Availability
- Accessibility
- Affordability
- Acceptability

- 70% of patients take treatment with out of pocket expenses
- Only 5% of patients have insurance cover
- 10-15% of patients covered by Government
- Variable number of patients can afford HCV treatment
Stepwise Barriers to HCV Treatment

HCV Infection

Barriers:
- Asymptomatic disease
- Poor awareness/education
- Lack of medical coverage
- MD failure to screen or test

~25%

Diagnosis

Barriers:
- Patient non-adherence
- MD failure to identify need for referral
- Logistical concerns
- Limited specialist availability

~50%

Referral to Specialist

Barriers:
- Patient fears and misunderstandings
- Stigmatization
- Substance abuse
- Psychiatric comorbidity
- Financial concerns
- Transportation / logistical concerns
- Communication difficulties

<30%

Treatment Initiation
HEPATITIS C: Current Practices in Indonesia

Rino Alvani Gani

Hepatobiliary Division
Department of Internal Medicine
Universitas Indonesia
Cipto Mangunkusumo Hospital
### Data in Indonesia

**Basic health research, 2007**

<table>
<thead>
<tr>
<th>Population</th>
<th>Total</th>
<th>Anti-HCV(+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12,715</td>
<td>1.7%</td>
</tr>
<tr>
<td>Female</td>
<td>14,821</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

**Hepatitis C cases according to age-group (2007-2012)**

- **Anti-HCV(+) 35,453 (0.7%)**

**Data in Indonesia**

- **2.5%**

---

Basic Health Survey – Ministry of Health 2013
Chronic hepatitis C in Indonesia

- 1-2% of Indonesia population (~ 3.5 million people) were infected with HCV
- 60-65% of infected people (~ 2 million) were genotype 1 HCV
- 20-25% of infected people (~ 474,000 people) were progressed into cirrhosis in 15-20 years
- 1-4% of infected people (~ 14,000 people) were progressed into hepatoma

1. Hepatitis C National Surveillance data (October 2007 - September 2009)
2. Study of chronic hepatitis C prevalence in health care professionals, 2008
Current Indonesia Guideline of Hepatitis C Management
KONSENSUS NASIONAL PENATALAKSANAAN HEPATITIS C DI INDONESIA

PERHIMPUNAN PENELITI HATI INDONESIA
2014

PEDOMAN NASIONAL PELAYANAN KEDOKTERAN

HEPATITIS C

KEMENTERIAN KESEHATAN RI
2014
Standard treatment

Peg-Interferon + Ribavirin
Dual therapy algorithm for genotype 1 & 4

RNA VHC: Negatif (RVR) → Positif

- RNA VHC Negatif (RVR) → Positif
  - (Penurunan <2 log (NR))
  - Hentikan terapi
  - Positif (PR)

RNA VHC Positif
  - (Penurunan >2 log)
    - Negatif (DVR)
    - Durasi terapi 72 minggu

EVR: Negatif
  - Durasi terapi selama 24 minggu
    - (apabila viral load awal <400.000-800.000 IU/mL)
    - Terapi selama 48 minggu

Peg-IFN/RBV
Triple therapy algorithm with boceprevir (BOC) using response guided therapy (RGT)

**Peg-IFN/RBV**

- **Minggu ke-4**
  - RNA VHC Tidak Terdeteksi (ER)

**Peg-IFN/RBV + BOC**

- **Minggu ke-8**
  - Tidak Terdeteksi (ER)
- **Minggu ke-12**
  - Tidak Terdeteksi (ER)
  - **Minggu ke-24**
  - Durasi terapi 24 minggu*

**Ket:**
- ER → Early Response
- LR → Late Response
- *** → Stop Terapi

*hanya untuk fibrosis stadium F0-F3 ( naïve dan relapser)

*Stadium fibrosis dan terhadap respons dengan terapi BOC sebelumnya

**Perhimpunan Peneliti Hati Indonesia. Konsensus Penatalaksanaan Hepatitis C di Indonesia, 2014.**
Dual therapy algorithm for genotype 2, 3, 5 and 6

Monitor treatment response

1. Shorten duration for rapid responders (eRVR)
   ➡️ ↑ tolerability

2. Increase duration for slow responders (no eRVR)
   ➡️ ↑ Efficacy

3. Stop if no response (Futility rules)
   ➡️ ↑ cost-effectiveness
   ➣ ↓ DAA resistance
High SVR Rate for Indonesian (2013)
*Cure rate: 73-89%*

Studi Prospective observational study dari Juni 2003-September 2012 dari 80 (genotype 1&4) & 37 (genotype 2&3) from patients in Jakarta

Source: Andri Sulaiman, dr., SpPD-KGEH, Oral presentation,: Does the current SOC still meets its risk-benefit ratio for Chronic Hepatitis C, KONAS PPHI 2013, Manado
Current SVR with Peg-IFN + Riba

- Current SVR with Peg-IFN + Riba treatment in Indonesia:
  - Genotype 1: 65-83%
  - Genotype 2/3: 74-95%
  - Genotype 4: 51-66%
  - Genotype 5/6: 58-82%
  - Hemodialysis: 50-73%
  - HIV-HCV Co-infection: 61-66.7% (depends on genotype)

- Treatment access available through National Health Insurance
Evolving Treatment Access

- Indonesia → one of 90 countries that can have access to generic Sofosbufir and Ledispravir
- Interferon-free treatment → Next year
Conclusion

• Indonesia has a moderately high prevalence of hepatitis C patients
• Access of treatment can be achieved through National Health Insurance
• SVR with Peg-IFN + Riba is good
• Near future → Interferon free treatment
Thank You
Upcoming Treatment for Hepatitis C
Evolving of hepatitis C treatment
Evolving of hepatitis C treatment

Past
- HCV GT1–6
  - Peg-IFN/RBV

Present
- GT1
  - Triple | PI + P/R
  - Peg-IFN/RBV (?)
- GT2–6
  - Peg-IFN/RBV

Future
- IFN-free
  - 1 DAA ± RBV
  - 2 DAAs ± RBV
  - 3 DAAs ± RBV
- IFN-containing
  - Peg-IFN/RBV (?)
  - Triple | DAA + Peg-IFN/RBV
  - QUAD | 2 DAAs + Peg-IFN/RBV
Ideal regiment

- All oral
- Potent efficacy across all patient populations
- Pan-genotypic activity
- Short treatment duration
- High barrier to resistance
- Simple stopping rules and treatment algorithm
- Optimal safety/tolerability profile
- Low cost
- Optimal convenience
Direct Acting Antivirals (DAAs)
Specifically Targeted Antiviral Therapies for HCV (STAT-C): Directly Target the Virus

## DAA: Development Status

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug Class</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telaprevir</td>
<td>Protease Inhibitor</td>
<td>2011</td>
</tr>
<tr>
<td>Boceprevir</td>
<td>Protease Inhibitor</td>
<td>2011</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>Protease Inhibitor</td>
<td>November 2013</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>NS5B Nucleotide Inhibitor</td>
<td>November 2013</td>
</tr>
</tbody>
</table>

Available now in Indonesia
Upcoming Treatment

Fixed Dose
Ledispavir + Sofosbufir
Combination
(90 mg / 400 mg)

Expected to be available in Indonesia in mid 2016
Ledispavir – Sofosbuvir

- **Approved by FDA:** October 10, 2014
- **Indications:** chronic HCV genotype 1 in adults
- **Class and mechanism:**
  - Ledispavir: NS5A inhibitor
  - Sofosbuvir: Nucleotide analog NS5B polymerase inhibitor
- **Dosing:** FDC (90 mg/400 mg) once daily
## Ledispavir – Sofosbuvir

<table>
<thead>
<tr>
<th>Genotype 1 Patient Populations</th>
<th>Treatment Duration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naïve with or without cirrhosis</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment experienced** without cirrhosis</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Treatment experienced** with cirrhosis</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

*Consider treatment duration of 8 weeks in treatment-naïve patients without cirrhosis who have a pretreatment HCV RNA less than 6 million IU/mL.

**Treatment-experienced patients who have failed treatment with either (a) peginterferon alfa plus ribavirin or (b) HCV protease inhibitor plus peginterferon alfa plus ribavirin.

---

*Harvoni Prescribing Information. Gilead Sciences.*
### Ledispavir – Sofosbuvir

<table>
<thead>
<tr>
<th>Duration of Treatment</th>
<th>Estimated Cost*</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Weeks</td>
<td>$63,000</td>
</tr>
<tr>
<td>12 Weeks</td>
<td>$94,500</td>
</tr>
<tr>
<td>24 Weeks</td>
<td>$189,000</td>
</tr>
</tbody>
</table>

*Estimated cost based on Wholesaler Acquisition Cost in United States of $1125 per pill

*Harvoni Prescribing Information. Gilead Sciences.*
Government Regulation of Hepatitis C Treatment
Badan Penyelenggara Jaminan Sosial (Social Security Organizing Body)

• Several hepatitis treatments are covered by BPJS with specific terms and conditions applied
• Drugs covered by BPJS are regulated according to national formularium
Indonesia National Formularium

• **Adefovir dipivoksil**
  - Chronic hepatitis B with HBeAg (-) with low HBV DNA and high ALT
  - Not response to nucleos(t)ide analogues

• **Interferon alfa**
  - Available for hepatitis C patients
  - Can be use for melanoma patients

• **Lamivudin**
  - With HBV DNA examination
Indonesia National Formularium

- **Pegylated interferon alfa-2b**
  - Available for hepatitis C. Prescribed by gastroenterologist
- **Pegylated interferon alfa-2b**
  - Available for hepatitis B and C
- **Ribavirin**
  - Available for hepatitis C, complemented with interferon alfa
- **Telbivudin**
  - Available only for chronic hepatitis B
- **Tenofovir**
  - Must be prescribed by gastroenterologist
SVR rates in general

- All genotypes
- Genotype 1
- Genotype 2/genotype 3

<table>
<thead>
<tr>
<th>IFN monotherapy (weeks)</th>
<th>24</th>
<th>48</th>
<th>78</th>
<th>PEG-IFN</th>
<th>IFN + ribavirin</th>
<th>PEG-IFN + ribavirin</th>
<th>PEG-IFN + PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients achieving SVR (%)</td>
<td>6–19</td>
<td>11–19</td>
<td>10–22</td>
<td>18–39</td>
<td>35–43</td>
<td>61–79</td>
<td>76–82</td>
</tr>
</tbody>
</table>
Issues of Hepatitis C Treatment in Asia - Current Practices in Malaysia

HCV Round Table Discussion
Dr Tan Soek Siam
Hepatology Department
Selayang Hospital
Burden of Hepatitis C in Malaysia

• There is an estimated 453,700 people living with HCV infection in Malaysia in 2009 (2.5 % of adult population: 15-64 years old)

• 59% acquired HCV infection through injecting.

• Global Burden of Disease Study 2010 (Malaysia)

<table>
<thead>
<tr>
<th>Health Outcome</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HCV</td>
<td>16.574 (10.7624-26.2466)</td>
</tr>
<tr>
<td>Cirrhosis of liver secondary to hepatitis C</td>
<td>566.566 (464.108-725.255)</td>
</tr>
<tr>
<td>Liver cancer secondary to hepatitis C</td>
<td>771.221 (610.224-957.869)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,354.361</strong></td>
</tr>
</tbody>
</table>

Hepatitis C in Malaysia

In HD patients:
AntiHCV=6% in 2011 (20% in 2002)

Methadone Maintenance Clinics:
73% antiHCV + vs 17.2% antiHIV +

Aetiology: CHB =46.1%
(n=460) CHC =18.5%
Cryptogenic =15.4%
ALD =12.6%
Autoimmune =12.6%

Blood donors:
- n=3,540, anti-HCV + =1.49%
- n=6,495, Abbot HCV EIA v3.0 = 0.94%
  confirmation with 3rd gen RIBA = 0.14%.

PLHIV + data from Sg Buloh Hospital, ID center
(n=996): Anti-HCV + =16.87%

Multitransfused: Anti-HCV + = 5.8-22.4%

HCV cases assessed for treatment

- Self reported risk behaviours: two most common risks are previous blood or blood product transfusion (41.2-46.3%) and IDU (22-35.3%)
- Mean age 2003-2013 (n=644)
HCV genotypes- 5 centres across Malaysia

<table>
<thead>
<tr>
<th>Centre / Region</th>
<th>Year</th>
<th>N</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>G6</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMMC</td>
<td>2008-2014</td>
<td>419</td>
<td>153 (36.5%)</td>
<td>7 (1.7%)</td>
<td>257 (61.3%)</td>
<td>1 (0.2%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Selayang Hospital</td>
<td>2003-2013</td>
<td>644</td>
<td>252 (39.1%)</td>
<td>3 (0.5%)</td>
<td>382 (59.3%)</td>
<td>4 (0.6%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Kuantan and Temerloh, Pahang</td>
<td>2013-2014</td>
<td>154</td>
<td>42 (27.3%)</td>
<td>0</td>
<td>110 (71.4%)</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Alor Setar, Kedah</td>
<td>2007-2014</td>
<td>250</td>
<td>84 (33.6%)</td>
<td>0</td>
<td>159 (63.6%)</td>
<td>5 (1.9%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Ampang Hospital</td>
<td>Not specified</td>
<td>52</td>
<td>13 (25%)</td>
<td>1 (1.9%)</td>
<td>38 (73.1%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total, n=1519: GT3 = 62.3%
GT1 = 35.9%
GT4 = 0.7%
GT2 = 0.6%
GT6 = 0.4%

Source: MyC2C
Approved Anti-HCV treatments

• Licensed therapies:
  - Conventional interferon alfa, Pegylated interferon alfa, Ribavirin and Boceprevir

• Availability of treatment:
  - Public sector (all fully reimbursed except for boceprevir; specific number of allocations/year)
  - University (FOC for government servants)
  - Private sector (out of pocket)
SOC in public sectors hospitals

• Clinical assessment
• Bloods-FBC, LFT, RP, ANA, TFT, HCV RNA, HCV genotype, US, liver fibrosis assessment-liver biopsy (not done in some patients esp pt’s refusal/genotype 3), TE-limited to certain hospitals.
• Treatment-Pegylated interferon and Ribavirin is the SOC (Selayang Hosp-since 2004).
• FU-2 week, 4 weekly until end of treatment.
• Anemia is commonly managed by dose reduction ± blood transfusion. HD patients more likely to be given EPO
<table>
<thead>
<tr>
<th>Indications</th>
<th>Regimen and dose</th>
<th>Ribavirin</th>
<th>Duration</th>
</tr>
</thead>
</table>
| **Chronic Hepatitis C mono-infected and genotype 2 and 3** | S/C Pegylated interferon α-2a 180 mcg/week  
**OR** S/C Pegylated interferon α-2b 1.5 mg/kg/week | - 800 mg/day  
- If BMI > 25 or there is evidence of insulin resistance or metabolic syndrome or severe fibrosis or cirrhosis or older age use 15 mg/kg BW/day | Usually 24 weeks.  
48 weeks if have bridging fibrosis or cirrhosis and metabolic syndrome. |
| **Chronic Hepatitis C mono-infected and genotype 1 and 4** | S/C Pegylated interferon α-2a 180 mcg/week  
**OR** S/C Pegylated interferon α-2b 1.5 mg/kg/week | 15 mg/kg BW/day (in 2 divided doses) | Usually 48 weeks.  
24 weeks if G1 with LVL < 400,000 iu/ml, RVR and less than bridging fibrosis.  
72 weeks maybe needed in those with delayed response |
| **Chronic Hepatitis C co-infected with HIV and all genotypes** | S/C Pegylated interferon α-2a 180 mcg/week  
**OR** S/C Pegylated interferon α-2b 1.5 mg/kg/week | For all Genotype use Ribavirin at 15 mg/kg BW/day | Usually 48 weeks regardless of genotype.  
24 weeks-if G2/G3 with RVR+baseline VL < 400,000 iu/ml +less than bridging fibrosis. |
| **Chronic Hepatitis C on hemodialysis and all genotypes** | S/C Standard Interferon α-2b 3 MIU three times/week after hemodialysis  
*PEG and low dose RBV with frequent Hb monitoring* | No need Ribavirin | 48 weeks |
Treating CHC-what are our results?

Patients received treatment between 2000-2006 (Selayang) \(^1\)
- \(N = 76\), stdIFN/RBV or PEG/RBV
- Overall SVR = 72.3%
- Early discontinuation = 9.2%

Audit 2009 (Selayang), PEG/RBV
- Overall SVR = 67%
- Genotype 3 was higher at 79% compared to genotype 1 at 43%.

Audit 2012 (Selayang), PEG/RBV (n=126) \(^2\)
- SVR = 72.9% for GT3 and 35.1% for GT1

1. SSTan et al APASL 2006
2. Noor Aliza et al APASL 2015
Treating HIV/HCV co-infected

45 HIV/HCV coinfected pts were assessed. 44 took up PEG/RBV and completed by end of 2011.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years; median(IQR)</td>
<td>41 (37,47)</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>Male : 44 (98%)</td>
</tr>
<tr>
<td>IDU as risk behaviour</td>
<td>35 (77.8%)</td>
</tr>
<tr>
<td>Receiving ARV (%)</td>
<td>34 (75.5%)</td>
</tr>
<tr>
<td>CD4 (cells/uL); median (IQR)</td>
<td>492 (376; 621)</td>
</tr>
<tr>
<td>Fibrosis based on liver biopsy</td>
<td>Liver cirrhosis : 10%</td>
</tr>
<tr>
<td></td>
<td>Significant fibrosis : 50%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall (n=44)</th>
<th>Genotype (n=12)</th>
<th>1</th>
<th>Genotype (n=32)</th>
<th>3</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETR</td>
<td>32/44 (72.7%)</td>
<td></td>
<td>26/32 (81.3%)</td>
<td></td>
<td>0.038</td>
</tr>
<tr>
<td>SVR</td>
<td>28/44 (63.6%)</td>
<td></td>
<td>23/32 (71.9%)</td>
<td></td>
<td>0.064</td>
</tr>
</tbody>
</table>

- Rx completion rate=79.5%
- 15.9% drop out due to AE or default
- 4.6% due to lack of EVR

SSTan et al APASL 2013
100% reported one or more AE
85.3% of them were treated with EPO (2000–14 000 U/week), yet clinically significant anaemia developed in 70.6% of patients.
32% drop out rate.
272 consecutive HCV (1 Jan-31 Mar 2012) and FU x 2 yrs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results (n=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD (years)</td>
<td>47.7±11.8 years</td>
</tr>
<tr>
<td>Gender</td>
<td>74.6% male</td>
</tr>
<tr>
<td>Top 2 self reported risk factors</td>
<td></td>
</tr>
<tr>
<td>IDU (34.9%)</td>
<td></td>
</tr>
<tr>
<td>blood products transfusion (30.5%)</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>37.5%</td>
</tr>
<tr>
<td>Mean CTPS= 6.8±2.3</td>
<td></td>
</tr>
<tr>
<td>Mean MELD = 12.7±5.8</td>
<td></td>
</tr>
<tr>
<td>2 years FU (n=206)</td>
<td>13.1% died</td>
</tr>
<tr>
<td></td>
<td>9.7% developed new complications from cirrhosis</td>
</tr>
<tr>
<td>Assessment of liver fibrosis</td>
<td>•F0-F2(51.2%), F3-F4(39.5%), F5-F6(9.3%).</td>
</tr>
<tr>
<td>•HAI Fibrosis, LBx (n= 86)</td>
<td>•14.96 ±12.8 kPa</td>
</tr>
<tr>
<td>•LSM, TE (mean ± SD, n=123)</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>•Patients refusal (n=12), platelet&lt; 80,000 (n=21), decompensated cirrhosis or CTPS score &gt;8 (n=36), psychiatric co-morbidities (n=8), medical co-morbidities and others/physicians decision (n=45).</td>
</tr>
<tr>
<td>•Not treated (n=146, 53.7%)</td>
<td></td>
</tr>
<tr>
<td>•PEG/RBV (n=126, 46.3%)</td>
<td></td>
</tr>
</tbody>
</table>

Noor Aliza et al APASL 2015
Summary

• The prevalence of HCV in Malaysia is about 2.5% of adult population and varies between 6-73% (antiHCV+) in those with risk factors.

• For those assessed for treatment:
  – young age at early to mid forties.
  – two main risk factors for HCV infection are previous blood/blood product transfusion and IDU.
  – predominant genotypes are GT3 follow by GT1, they are found in 98% of cases with roughly 2 to 1 ratio.
Summary

• In the public sector, the current SOC is mainly dual therapy with PR.
• Reasonable SVR can be achieved in GT3 (even in ESRD and HIV/HCV co-infected patients) however it is unsatisfactory in GT1.
• In a tertiary liver centre: more than 1/3 are cirrhotics and slight more than half of our patients were not treated with PR for various reasons.
Thank you
Issues of Hepatitis C Treatment in Asia; Myanmar

Prof. Khin Maung Win
Honorary Professor
Department of Hepatology
University of Medicine 1
Ministry of Health
Yangon, Myanmar

Singapore Hepatitis Conference 2015
Disclosure

I have nothing to disclose.
## SEROPREVALENCE OF HCV

<table>
<thead>
<tr>
<th>Country</th>
<th>Study pop</th>
<th>Anti-HCV(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>Paid bld donors</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Volunt bld donors</td>
<td>0</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Volunt bld donors</td>
<td>3.4</td>
</tr>
<tr>
<td>Japan</td>
<td>Community</td>
<td>1.5</td>
</tr>
<tr>
<td>Korea</td>
<td>Community</td>
<td>1.7-5.7</td>
</tr>
<tr>
<td>Myanmar</td>
<td>Community</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>Voluntary bld donors</td>
<td>2.6</td>
</tr>
<tr>
<td>Pakistan</td>
<td>Community</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Bld donors</td>
<td>0.1-20.7</td>
</tr>
<tr>
<td>Thailand</td>
<td>Bld donors</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Prevalence of HBV-DNA and HCV-RNA in Primary Liver Cancer (YGH)

- HBV-DNA: 46.2%
- HCV-RNA: 23.1%
- ALL(-): 30.8%
<table>
<thead>
<tr>
<th>Genotype</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1</td>
<td>135</td>
<td>11%</td>
</tr>
<tr>
<td>Genotype 2</td>
<td>12</td>
<td>1%</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>481</td>
<td>40%</td>
</tr>
<tr>
<td>Genotype 4</td>
<td>337</td>
<td>27%</td>
</tr>
<tr>
<td>Genotype 6</td>
<td>263</td>
<td>21%</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>1</td>
<td>0%</td>
</tr>
</tbody>
</table>

Total number = 1229
HCV Genotyping
Versant (LiPA 2.0)
2009 to 2012
Genotype 1
Total number = 263
Subtype 1b dominant

HCV Genotyping
Versant (LiPA 2.0)
from 2009 to 2012
Genotype 3
Total number = 481
Subtype 3b dominant

Singapore Hepatitis Conference 2015
IL28B Gene Polymorphisms in Myanmar Patients with Chronic HCV Infection Genotype 1
Treatment of HCV in Myanmar

- Immunomodulator
  - Pegylated Interferon Alfa-2a
  - Pegylated Interferon Alfa-2b
- Ribavirin
- DAA
  - Sofosbuvir
Optimal treatment

• Currently pegylated interferon and ribavirin combination is the standard of care for chronic hepatitis C infection in Myanmar.
• Recently generic SOFOSBUVIR is available.
Multiple Direct Acting Antivirals

5’ UTR -> Core E1 E2 S NS2 NS3 3 NS4B NS5A NS5B 3’ UTR

- Protease
- Polymerase

HCV Pls

Viral enzyme
Active site
Telaprevir
Boceprevir
Simeprevir
Faldaprevir
Asunaprevir
ABT-450
MK-5172
Sovaprevir
ACH-2684

NS5A inhibitors
Non-enzyme
Replication complex
Daclatasvir
Ledipasvir
ABT-267
GS-5816
ACH-3102
PPI-668
GSK2336805
Samatasvir
MK-8742

NS5A Nuc inhibitors
Viral enzyme
Active site
Sofosbuvir
VX-135
IDX20963
ACH-3422

NS5B Non-nuc inhibitors (NNI)
Viral enzyme
Allosteric site
ABT-333
Deleobuvir
BMS-791325
PPI-383
GS-9669
TMC647055
Only SOFOSBUVIR is available in Myanmar
AASLD-IDSA guidelines

Revised Date: March 21, 2014

PEG IFN eligible
  • SOF + PEG IFN + RBV 12 weeks

PEG IFN ineligible
  • SOF + RBV 24 weeks
SOFOSBUVIR Myanmar Experience

- 236 patients have been treated
- RVR 100%
- ETR and SVR awaiting
- Adverse reactions are due to PEG IFN or RBV
- Expect to have Sofosbuvir + Ledipasvir or Daclatasvir in a year time
This guidelines should be a useful and practical reference for Myanmar physicians and general practitioners treating patients with chronic HCV infection.
Ledipasvir or Daclatasvir
Who should be treated?
Priority ????
Widespread and indiscriminate use of DAA may lead to emergence of DAA resistance
My Team

Thank You

Singapore Hepatitis Conference 2015
Hepatitis C Infection In Singapore

Richard Guan
MBBS, MRCP(UK), FAMS(Gastro), FRCP(Edin), FRCP(Lond)
Gastroenterologist & Hepatologist, Mt Elizabeth Medical Centre, Singapore
Summary of HCV treatment practice in the AP region

- Physicians *not likely* to perform a liver biopsy on HCV patients at diagnosis.
- *Seromarkers* (not liver biopsies) are used to determine fibrosis.
- *HCV-RNA testing* and *viral genotyping* are not used as often in treatment monitoring as in other parts of the world.
- Physicians *more likely* (like in Latin America) to start antiviral treatment *within 3 months* of an HCV diagnosis.
- 80% consult National Guidelines; Other guidelines also referenced by a substantial proportion of physicians (AASLD: 52%, APASL: 41%, EASL: 38%)
- 1/3 patients decline SOC (PegIFN + Ribavirin) therapy. (Significantly higher than in other parts of the world)
- Cost of medicines is the topmost, patient-related barrier to treatment in the Asia Pacific region. Insufficient government funding high up on the list.

From a recent worldwide survey by I-C3/Kromite
Population of Singapore (as of June 2013):

- Singaporeans: 3.3 million (61.4%)
- Permanent residents: 531,200 (9.8%)
- Foreigners: 1.6 million (28.8%)

Multi-ethnic (data based only on resident population)

- Chinese: 74.2%
- Malays: 13.3%
- Indians: 9.2%
- Others: 3.3%
## HCV Prevalence and Genotype Distribution
### Central Asia, South East Asia & Australia Pacific

<table>
<thead>
<tr>
<th>Country</th>
<th>Community</th>
<th>Blood Donors</th>
<th>CLD</th>
<th>HCC</th>
<th>Dialysis</th>
<th>IDU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>2.3</td>
<td>0.4</td>
<td></td>
<td></td>
<td>3.5</td>
<td>37-74</td>
</tr>
<tr>
<td>China</td>
<td>1 (up to 30)</td>
<td>0.3</td>
<td>7-17</td>
<td></td>
<td>18.2</td>
<td>46-95</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>0.5</td>
<td>0.08</td>
<td>0.7</td>
<td>8</td>
<td>8.2-45</td>
<td>92</td>
</tr>
<tr>
<td>India</td>
<td>1.85</td>
<td>1.8</td>
<td>10-48</td>
<td>10-15</td>
<td>63-4</td>
<td></td>
</tr>
<tr>
<td>Indonesia</td>
<td>2.1-2.3</td>
<td></td>
<td></td>
<td></td>
<td>63.4</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>1.6-28</td>
<td></td>
<td></td>
<td>83</td>
<td>30-40</td>
<td></td>
</tr>
<tr>
<td>Korea</td>
<td>1.7</td>
<td>1.3</td>
<td></td>
<td>9.3-28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaysia</td>
<td>1.6</td>
<td>1.5</td>
<td></td>
<td>23</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>1.6</td>
<td>0.87</td>
<td></td>
<td>3.5</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Nepal</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>94</td>
<td>90</td>
</tr>
<tr>
<td>Pakistan</td>
<td>6</td>
<td>0.13-5</td>
<td>60-70</td>
<td>50</td>
<td>23.6-8</td>
<td>64</td>
</tr>
<tr>
<td>Philippines</td>
<td>0.94</td>
<td>0.33-2.3</td>
<td></td>
<td></td>
<td></td>
<td>72</td>
</tr>
<tr>
<td>Singapore</td>
<td>1.7</td>
<td>0.54</td>
<td></td>
<td>31</td>
<td>20</td>
<td>42.5</td>
</tr>
<tr>
<td>Taiwan</td>
<td>4.4 (0.4-10)</td>
<td>0.8</td>
<td></td>
<td>29.5</td>
<td>95.3</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>3.2-5.6</td>
<td>~6.5</td>
<td></td>
<td></td>
<td>30-40</td>
<td>90</td>
</tr>
</tbody>
</table>

Prevalence (Viremic): 0.0% - 0.6%
0.6% - 0.8%
0.8% - 1.3%
1.3% - 2.9%
2.9% - 7.8%

Data on file: Merck

HCV Infection in Singapore

Mt Elizabeth MC (n=237)

Indonesians: 47
Myanmese: 32
Kampuchians: 6
Malaysians: 3
Singaporeans: 4
Others: 3

Countries where our HCV patients come from

Myanmar
Cambodia

Indonesia
Malaysia

Changi GH (n=63)

Myanmese: 15
Kampuchians: 40
Malaysians: 5
Singaporeans: 3
Others: 1

India
Mongolia
Singapore
HCV Infection in Singapore

### Epidemiology

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Overall chronic HCV prevalence approx 1.0 % of country's population representing about 50,000 individuals infected.</td>
</tr>
<tr>
<td>2</td>
<td>Total diagnosed population</td>
</tr>
</tbody>
</table>

### Risk Factors For Transmission For Hep C In Asian Pacific Region

- Blood and blood products from paid donations
- Intravenous drug use
- Traditional therapies including acupuncture, suidama, tattooing
- Medical practices using non disposable glass syringes and needles
- The lack of universal screening of blood donors in some parts
- Lack of universal precautions during haemodialysis
- Mother to baby transmission
- Sexual transmission
HCV Infection in Singapore

### Epidemiology

<table>
<thead>
<tr>
<th></th>
<th>Overall chronic HCV prevalence approx 1.0 % of country's population representing about 50,000 individuals infected.</th>
<th>Prevalence trend is presumably steady</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Total diagnosed population</td>
<td>Approx. 5000 patients.</td>
</tr>
</tbody>
</table>

**Risk Factors For Transmission For Hep C In Asian Pacific Region**

- Blood and blood products from paid donations
- Intravenous drug use
- Traditional therapies including acupuncture, suidama, tattooing
- Medical practices using non disposable glass syringes and needles
- The lack of universal screening of blood donors in some parts
- Lack of universal precautions during haemodialysis
- Mother to baby transmission
- Sexual transmission

✓ Risk factors present in Singapore
## HCV Infection in Singapore

### Epidemiology

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<table>
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<td></td>
<td>Approx. 5000 patients.</td>
</tr>
<tr>
<td>3</td>
<td>Genotype distribution within the country:</td>
</tr>
<tr>
<td></td>
<td>G1a/b: 80%</td>
</tr>
<tr>
<td></td>
<td>G2: 7%</td>
</tr>
<tr>
<td></td>
<td>G3: 15%</td>
</tr>
<tr>
<td></td>
<td>G4/5/6: 3%</td>
</tr>
</tbody>
</table>

### Patient Distribution

- **Mt Elizabeth MC (n=237)**
  - HCV1a: 46
  - HCV1b: 5
  - HCV2: 22
  - HCV3: 14
  - HCV4: 6
  - HCV5: 6
  - HCV6: 10
  - Mixed: 1

- **Changi GH (n=63)**
  - HCV1a: 43
  - HCV1b: 8
  - HCV2: 6
  - HCV3: 6
  - HCV4: 22
  - HCV5: 14
  - Indeterminate: 6

### Reasons for Not Recommending Treatment (P/R)

- N ALTs
- N Liver Bx
- Continuing IVDU
- Age >70yrs
- Poor Health
- Advanced Liver Disease
- Post renal transplant
## HCV Infection in Singapore

### Epidemiology

1. **Overall chronic HCV prevalence** approx 1.0 % of country's population representing about 50,000 individuals infected.  
   - Prevalence trend is presumably steady

2. **Total diagnosed population**  
   - Approx. 5000 patients.

3. **Genotype distribution within the country:**  
   - G1a/b: 80%  
   - G2: 5%  
   - G3: 15%  
   - G4/6: 5%

4. **Of the PREVALENT HCV population approximately:**  
   - co-infection with HIV < 10%.  
   - co-infection with HBV 10%  
   - Possible steady trend

5. **Current distribution of diagnosed patients:**  
   - 50% treatment naïve; 50% treatment experienced

6. **Treatment (P/R) was not recommended for approx. 20% of patients diagnosed for the following reasons:**  
   - N ALTs; N Liver Bx;  
   - Continuing IVDU;  
   - Age >70yrs; Poor Health;  
   - Advanced Liver Disease; Post renal transplant
# HCV Infection in Singapore

## Current Treatment Paradigm

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td>Who treats chronic HCV patients?</td>
<td>Gastros / ID Physicians</td>
</tr>
</tbody>
</table>
| **2** | Access to care? Readily available | • Walk in.  
• Referred by PHC physicians |
| **3** | Diagnostic processes followed prior to the initiation of treatment? | Clinical assessment, HCV genotype / load, LFT, Renal Panel, CBC, TFT + Thyroid Ab, Pregnancy tests, Cardiac and Psychiatric assessments if necessary |
| **4** | Tests done to stage/grade liver disease? | Liver Ultrasound, Fibroscan, LFT, CBC, Liver biopsy |
| **5** | Tests/procedures used to guide treatment? | CBC, LFT, TFT, RP, US Pregnancy tests, HCVRNA |
| **6** | The present treatment for treatment naïve patients: PegIntron 1.5ug/kg weekly + Ribavirin 800-1200 mg daily OR Pegasys 180ug weekly + Ribavirin 800-1200 mg daily. Cost of (P/R)treatment: US$ 8000 to US$ 16000 | Treatment period: GT 1/4/6 12 mo, GT2 6 mo, GT3 6 - 9 mo. |
# HCV Infection in Singapore

## Current Treatment Paradigm

<table>
<thead>
<tr>
<th></th>
<th>Evaluation of treatment success?</th>
<th>Response guided approaches used?</th>
<th>SVR 24 RVR, EVR</th>
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<td>Evaluation of treatment success?</td>
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<td>8</td>
<td>Treatment is refused by approx. 40% of diagnosed patients for the following reasons:</td>
<td>Costs; Perceived side effects; N LFT.</td>
<td>SVR by HCV Genotype</td>
</tr>
<tr>
<td>9</td>
<td>Treatment outcomes (P/R):</td>
<td>SVR by HCV Genotype</td>
<td>SVR by HCV Genotype</td>
</tr>
<tr>
<td></td>
<td>• Sustained viral responders (cured)</td>
<td>G1 approx 80%</td>
<td>G1 approx 80%</td>
</tr>
<tr>
<td></td>
<td>• partial responders</td>
<td>GT2 approx 90%</td>
<td>GT2 approx 90%</td>
</tr>
<tr>
<td></td>
<td>• nonresponders</td>
<td>GT3 approx 70%</td>
<td>GT3 approx 70%</td>
</tr>
<tr>
<td></td>
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<td>Prominent co-morbidities that affect treatment (P/R) decisions/outcomes:</td>
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<td>Of the TREATED HCV (P/R) population approximately:</td>
<td>20% IFN intolerant 30% Ribavirin intolerant 5% IFN contra-indicated &lt;5% Ribavirin contra-indicated.</td>
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Pegylated Interferon and Ribavirin treatment for hepatitis C: A local ASIAN experience (Singapore)

Patients:
165 consecutive patients with chronic Hepatitis C infection treated at a specialist clinic between 2003 and 2007.
95 m: 70 f.
Age range: 24 - 70 yrs old. median: 46 yrs
Genotypes 1 - 6

Dosages:
Weight based PegIFN a2b or Flat dose PegIFN a2a weekly and Ribavirin 1 – 1.2G daily. Length of Tx depends on genotype

Results:
Interferon/ Ribavirin related side effects common necessitating lowering of doses in up to 60% patients and non completion of treatment in 5/27 patients.

27 patients (16%) did not complete treatment
138 patients analysed
Pegylated Interferon and Ribavirin treatment for hepatitis C: A local ASIAN experience (Singapore)

Results:

Proportions of patients who completed treatment:
- Tx complete: 84%
- Absconded: 3%
- Tx stopped due to side effects: 13%

Treatment Response:
- RVR: 60%
- EVR: 18%
- Responders: 15%
- Non response: 7%
Pegylated Interferon and Ribavirin treatment for hepatitis C: A local experience (Singapore)

Results:

Response to HCV Treatment

% patients

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<th>EVR 3mo</th>
<th>ETVR</th>
<th>Non Response</th>
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<td>Response</td>
<td>85</td>
<td>93</td>
<td>7</td>
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Pegylated Interferon and Ribavirin treatment for hepatitis C: A local experience (Singapore)

Results:

![Response to HCV Treatment](chart.png)
## HCV Infection in Singapore

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<td>GT2  approx 90%</td>
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<td>&lt;5%Ribavirin contra-indicated</td>
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<tr>
<td>13</td>
<td>For those patients that failed P/R,</td>
</tr>
<tr>
<td>14</td>
<td>The present (re)treatment for treatment experienced patients:</td>
</tr>
<tr>
<td>15</td>
<td>Unmet treatment needs with the current SOC (P/R)</td>
</tr>
<tr>
<td>16</td>
<td>Current access and reimbursement for HCV products? What testing and therapy is reimbursed and what is not?</td>
</tr>
<tr>
<td>17</td>
<td>Treatment Guidelines NO National Guidelines.</td>
</tr>
</tbody>
</table>
# HCV Infection in Singapore

<table>
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<tr>
<th>Doctor/Public Education, Diagnosis &amp; Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education</strong></td>
</tr>
<tr>
<td>1 Education programs for health care workers</td>
</tr>
<tr>
<td>2 Public education programs</td>
</tr>
<tr>
<td>Inadequate</td>
</tr>
</tbody>
</table>

| **Diagnosis**                                 |
| 1 Universal anti-HCV testing                  |
| 2 Anti-HCV testing for donated blood           |
| No                                           |
| Mandatory                                    |

| **Prevention**                                |
| 1 Anti-HCV testing for donated blood/blood products. |
| 2 Disposable needles encouraged for all procedures |
| 3 Separate haemodialysis machines for HCV viraemic patients |
| 4 General universal precautions                |
| Mandatory                                    |
| Yes                                          |
| Yes                                          |
## HCV Infection in Singapore

### The Future Is Here

<table>
<thead>
<tr>
<th></th>
<th>Shorter IFN based therapy available (NPB)</th>
<th>IFN free therapies available: (NPB)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Broceprevir + PIFN + Ribavirin (US$ 30,000)</td>
<td>Sofosbuvir + Ribavirin (US$ 65,000)</td>
<td>7mo for GT1</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir + PIFN + Ribavirin (US$ 68,000)</td>
<td>Sofosbuvir + Ledipasvir (US$ 75,000)</td>
<td>3mo for most GT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sofosbuvir + Daclatasvir (US$ 87,000)</td>
<td>3-6 mo depending on GT and presence/absence cirrhosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Daclatasvir + Anusoprevir (US$ 64,000)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ombitasvir + Paritaprevir/ritonavir + Dasabuvir (US$ 59,000)</td>
<td></td>
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</table>
# HCV Infection in Singapore

<table>
<thead>
<tr>
<th>Triple Therapy:</th>
<th>P/R + Broceprevir</th>
</tr>
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<tbody>
<tr>
<td>Patients and Methods</td>
<td></td>
</tr>
<tr>
<td>n =13</td>
<td>11 m; 2 f.</td>
</tr>
<tr>
<td></td>
<td>3 GT1a: 10 GT1b</td>
</tr>
<tr>
<td></td>
<td>RGT (Max 48wks)</td>
</tr>
</tbody>
</table>

## Results

- **5 P/R null responders**
- **4 P/R relapsers**
- **4 treatment naïve**

| Null responders (n=5) | 1 responded (no cirrhosis); 1 relapsed |
| Relapses (n=4) | 4 responded |
| Treatment naïve (n=4) | 1 responded (no cirrhosis); 1 nonresponded; 2 absconded |

- **6 responded (SVR6mo), 1 relapsed**, 3 nonresponders, 3 absconded

## Conclusion/Impression

- Shortened treatment time in treatment naïve
# HCV Infection in Singapore

<table>
<thead>
<tr>
<th>Triple Therapy:</th>
<th>P/R + Sofosbuvir</th>
</tr>
</thead>
</table>

**Patients and Methods**

<table>
<thead>
<tr>
<th>n = 3,</th>
<th>2 m; 1 f.</th>
<th>1 GT1a; 1 GT1b; 1 GT6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3 months therapy</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>3 patients</th>
<th>1 cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 responded</td>
<td></td>
</tr>
</tbody>
</table>

Side effects minimal; less than P/R therapy

**Conclusion/Impression**

There is still a place for short term IFN based triple therapy in AP
Apparently pangenotypic (like P/R)
Can be cheaper than IFN free therapy
HCV Infection in Singapore

IFN Free Therapy

Patients and Methods

N=19
13 previous non responders
12m : 7f
3 GT1a: 11 GT1b; 2 GT2; 2 GT3; 1 GT6
28 – 74 yrs
12 cirrhosis (2 GT1a, 5 GT1b; 2 GT2; 2 GT3; 1 GT6)

Medications:
Declatasvir, Ledipasvir, Sofobuvir, Simeprevir, Ribavirin, Ombitasvir/Paritaprevir/ritonavir/Dasabuvir (Vikeria Pak).

12 – 24 weeks therapy (Ref AASLD; EASL 2014/5)

Results

13/19 finished therapy to date

1 SOF+SMV+R x 12 wks (GT1b, cirrhosis) Relapse
1 SOF+DEC+R x 24wks (GT1b, cirrhosis) SVR8
4 SOF+LED+R x 12wks (1 GT1b; 2 GT1a; 1 GT6) (3 cirrhosis) 2ETR
6 SOF+R x 12(2)-24wks(4) (2 GT1b; 2 GT2; 2:GT3) (4 cirrhosis) 2ETR 3 SVR12 1 Relapse
5 SOF + LED x 8 – 24wks (GT1b. 2 cirrhosis) 2 SVR12
2 Viekira Pac+R x 12wks (1GT1b, 1GT1a. 1 cirrhosis) 1 SVR8
## IFN Free Therapy

### Results

- Minimal/no side effects

### Conclusions/Impressions

- Safe and well tolerated
- Most unmet treatment needs of the IFN era...met
- Cost is beyond the reach of most patients

Drs Wijaja Luman and Ivy Yap contributed patients
HCV Treatment....Singapore....2015

Thank you for your attention
Current Practice for Hepatitis C in Taiwan: Now and Near Future

Pei-Jer Chen
Hepatitis Research Center
National Taiwan University Hospital
A Survey of Anti-HCV from a National Nutrition Survey Subjects in Taiwan

• Bureau of Health Promotion, Taiwan

• Subjects: >15 y/o, 6588 cases, Feb. 2002
  – Randomly selected from 88 townships

<table>
<thead>
<tr>
<th></th>
<th>Case no.</th>
<th>Anti-HCV Positive rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>3159</td>
<td>3.39</td>
</tr>
<tr>
<td>Female</td>
<td>3429</td>
<td>4.32</td>
</tr>
<tr>
<td>Overall</td>
<td>6588</td>
<td>3.87</td>
</tr>
</tbody>
</table>

Hsu LC. et al, data from Bureau of Health Promotion 2003
Anti-HCV Positive Rate in Different Age Populations: (Total carriers about 700,000)
Evolution of IFN-based Therapies:

- **1991**: Standard IFN 6 mos
- **1998**: IFN 12 mos, IFN/RBV 6 mos
- **2001**: PegIFN 12 mos
- **2011**: PegIFN/RBV/DAA
- **2013**: DAAs Boceprevir or Telaprevir + P/R

**SVR (%)**

- IFN 6 mos: 6%
- IFN 12 mos: 16%
- IFN/RBV 6 mos: 34%
- IFN/RBV 12 mos: 42%
- PegIFN 12 mos: 39%
- PegIFN/RBV 12 mos: 55%
- PegIFN/RBV/DAA: 70+
- DAA + RBV ± PegIFN: 90+

Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.
Reduction of CHC patients by Treatment: Eligibility for First Line Antiviral Therapy for CHC in Taiwan: About 10,000 CHC cases treated a year

1. Pegylated interferon plus ribavirin is reimbursed since 2003
2. Anti-HCV positive, Abnormal ALT, and HCV RNA positive
3. No liver function decompensation.

Reaching RVR
Treatment for 24 weeks or less

No RVR, reaching EVR or pEVR
Treatment for 48 weeks

Stop treatment for those not reaching pEVR

Relapse

Retreatment with PegIFN and Ribavirin 48 weeks, if the first treatment was given for 24 weeks only.
The epidemiology of hepatitis C can be explained using a leaky bucket as an analogy.

New HCV Infections:

Cured cases

Mortality:

The dynamic of total HCV load in a country depends upon the increase of new HCV infections and the decrease of cured cases and the mortality.
Updated Annual new HCV infection in Taiwan: Confirmed anti-HCV seroconversion rate among repeated donors is 0.03% per year

Presumably there are at least 7000 new HCV infection a year in Taiwan
Dynamic of HCV disease load in Taiwan

- Anti-HCV seropositive cases: about 900,000 people
- HCV RNA positive: around 700,000 cases.
- New HCV infections: about 7000 cases a year.
- Treated cases: around 10,000 cases a year by P+R.
- Around 70% SVR, therefore curing about 7000 cases a year.
The epidemiology of hepatitis C can be explained using a leaky bucket as an analogy.

New HCV Infections: Ca. 7000 cases A year

Cured: About 7000 cases A year

Mortality: About 4000 cases Died of ESLD; And 4500 cases Of non-liver deaths A year

The Reduction of total HCV load in Taiwan depends upon the mortality of HCV cases (or ESLD or non-ESLD).

The total HCV disease load will not reduce significantly simply by current P+R therapies.
Unmet Needs for CHC Tx in Taiwan

Those who are ineligible to PegIFN/RBV

Those who are intolerant of PegIFN/RBV

Those who do not achieve SVR:

\[ 61823 \times (1 - 70\%) = 18546 \]
Direct-Acting Antivirals (DAAs)

Schinazi R et al., Liver Int 2014; 34 Suppl 1: 69-78.

Protease Inhibitors
- Telaprevir
- Boceprevir
- Simeprevir
- Faldaprevir
- Asunaprevir
- ABT-450
- MK-5172
- Sovaprevir
- ACH-2684

NS5A Inhibitors
- Daclatasvir
  - Ledipasvir
  - ABT-267
  - GS-5816
  - ACH-3102
  - PPI-668
  - GSK-2336805
  - Samatasvir
  - MK-8742

Polymerase Inhibitors
- Nucs
  - Sofosbuvir
  - VX-135
  - IDX-20963
  - 791325
  - ACH-3422
- Non-Nucs
  - PPI-383
  - GS-9669
  - TMC-647055

5'NTR
- Capsid
- Envelope Glycoproteins
  - C
  - E1
  - E2

Structural proteins
- NS1
- NS2

Nonstructural proteins
- Metalloprotease
- Serine protease
- RNA helicase
- Cofactors
  - NS3
  - NS4A
  - NS4B
  - NS5A
  - NS5B

3'NTR
- RNA Polymerase
First IFN-DAAs curing HCV: Al447011 (DUAL): DCV + ASV

Sentinel Cohort Study Design

Group A (n = 11)

DCV 60 mg QD + ASV 600 mg BID

Follow-up (up to 48 Weeks post-treatment)

Group B (n = 10)

DCV 60 mg QD + ASV 600 mg BID + alfa/RBV

Follow-up (up to 48 Weeks post-treatment)

24 Weeks
Summary of SVR(%) by cohort (mITT)

168/205
192/235
182/203
First IFN-free DAAs Approved in Asia

- Daclatasvir and Asunaprevir approved for GT1b CHC in Japan in September 2014, and reimbursed by their health insurance.
Baseline NS5A SNPs Affect SVR rates

Daclatasvir/Asunaprevir

IFN+/-RBV Intolerable or Ineligible

Null Response

Guideline for HCV treatment, ed. 3.2, 2014, JSH
Proposed Treatment Options for HCV Infection in Taiwan: Building upon Japan’s Model

• **GT 1b**
  - PegIFN/RBV
  - Null/partial responders to P/R or ineligible/intolerant
  - Daclatasvir / Asunaprevir
  - RAV to DCV/ASV
  - DCV/ASV + ?
  - Other DAAs

• **GT 2**
  - PegIFN/RBV
  - Null/partial responders to P/R or ineligible/intolerant
  - Sofosbuvir / weight-based RBV
HCV Round table discussion
Current practice in Asia
(Thailand)

Tawesak Tanwandee, MD.
Associate Professor of Medicine
Division of Gastroenterology, Siriraj Hospital,
Mahidol University, Bangkok, Thailand
Hepatitis C infection in Thailand

1.3%

4.5%

1.37%

0.5%

Chronic Hepatitis C in Thailand
Route of transmission of 405 HCV patients(%)
## First Time Blood Donors in Thailand

<table>
<thead>
<tr>
<th>Risks factors</th>
<th>Odds ratio (95% CI) Univariate</th>
<th>Odds ratio (95% CI) Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of blood transfusion</td>
<td>9.2 (5.8,14.4)</td>
<td>12.3 (7.6,19.9)</td>
</tr>
<tr>
<td>History of IDUs</td>
<td>64.2 (28,147)</td>
<td>61.5 (26.6,142.5)</td>
</tr>
<tr>
<td>Potential unsafe injection</td>
<td>6.9 (4.4,10.9)</td>
<td>3.3 (1.8,5.9)</td>
</tr>
<tr>
<td>Sharing of razors</td>
<td>2.6 (1.9,3.4)</td>
<td>2.3 (1.6,3.2)</td>
</tr>
<tr>
<td>Unsafe sex</td>
<td>2.3 (1.7,3.1)</td>
<td>1.6 (1.1,2.4)</td>
</tr>
</tbody>
</table>

95% of donors with history of IDU were positive for anti-HCV

Tanwandee T, J Med Assoc Thai. 2006
Blood donors screening

- Anti-HCV testing introduced 1991
- Multiplex NAT (HIV, HBV, HCV) introduced in January 2007
  - Anti HIV Ag/Ab combo
  - HBsAg/Anti-HBc
  - Anti HCV (3rd generation)
  - GenProbe (TIGRIS/Procleix Ultrio) and Cobas AmpliScreen

- NAT positive HCV were then confirmed by conventional RNA viral load and genotyping
- Risk of HCV infection less than 1:490,000 unit

Phikulsod S. et al. Transfusion 2009
Current HCV situation in Thailand

• About 1% or less in general population
• Mostly infection before 1990 from blood transfusion
  – Older patients, more advanced disease
• New infection can occur in minority (IDU subjects in Bangkok area)
HCV genotype distribution by country in Asia Pacific

China: Genotypes 1a, 2a, 2c, 3, 6
Korea: Genotypes 1a, 2b, 2a
Japan: Genotypes 1a, 2b, 3
Taiwan: Genotypes 1a, 2b, 3a
Thailand: Genotypes 1a, 2a, 2c, 3a, 3b
Australia: Genotypes 1a, 2, 3, 4, 6
India: Genotypes 1a, 4, 6
Pakistan: Genotypes 1a, 2a, 3a, 3b
Vietnam: Genotypes 1a, 3a, 3b

Treatment
# Result of HCV treatment with Peg/Riba in a patient at 30 year old (Thailand)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total cost</th>
<th>QALYs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV Genotype 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palliative care</td>
<td>783,000</td>
<td>14.75</td>
<td>-</td>
</tr>
<tr>
<td>Peg2a+RBV</td>
<td>740,000</td>
<td>16.75</td>
<td>-21,600</td>
</tr>
<tr>
<td>Peg2b(1.5)+RBV</td>
<td>792,000</td>
<td>15.85</td>
<td>7,600</td>
</tr>
<tr>
<td><strong>HCV Genotype 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palliative care</td>
<td>783,000</td>
<td>14.75</td>
<td>-</td>
</tr>
<tr>
<td>Peg2a+RBV</td>
<td>336,000</td>
<td>18.11</td>
<td>-133,000</td>
</tr>
<tr>
<td>Peg2b(1.5)+RBV</td>
<td>295,000</td>
<td>18.01</td>
<td>-149,000</td>
</tr>
</tbody>
</table>
Current Treatment of HCV in Thailand

- Peg/Riba is offered for free to naïve HCV patients who has significant liver disease including HIV co-infection
Cost-Effectiveness for Chronic Hepatitis C Virus Genotype 1 for Boceprevir-Based Regimen in Thailand

Number of events prevented per 10,000 patients by BOC/PR compared with PR Alone (% Reduction)

Thongsawat S. et al. manuscript submitted
## ICERs BOC/PR vs. PR48

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Treatment Naïve Patients</th>
<th>Treatment Experienced Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cost</td>
<td>QALYs</td>
</tr>
<tr>
<td>PR</td>
<td>914,760</td>
<td>13.30</td>
</tr>
<tr>
<td>BOC/PR</td>
<td>836,430</td>
<td>13.95</td>
</tr>
<tr>
<td>F0-F3: PR</td>
<td>912,990</td>
<td>13.45</td>
</tr>
<tr>
<td>F4: PR</td>
<td>948,389</td>
<td>10.50</td>
</tr>
<tr>
<td>F4: BOC/PR</td>
<td>1,343,506</td>
<td>10.63</td>
</tr>
</tbody>
</table>

Thongsawat S. et al. manuscript submitted
Boceprevir is currently offered for HCV genotype 1
(but only for the government employees)
New DAAs

• Sofosbuvir, Sofosbuvir/Ledipasvir, Simeprevir, and Daclatasvir are under reviewed by Thai FDA
• More likely to replace Peg/Ribavirin soon
• SOF/PR or Sofosbuvir/daclatasvir might fit Thailand situation where HCV genotype 1, 3, 6 are prevalence
• With the effort of WHO to provide essential drugs for HCV, we hope that the benefit will come to Asia
Conclusion

• Prevalence of chronic hepatitis C infection in Thailand has decreased steadily over time
  – blood donors screening and decrease use of intravenous drug
• Treatment for chronic hepatitis C currently has been offered to all patients
• With all of these effort, we hope that complication of chronic liver disease and HCC will be reduced.
The 4th ASEAN Perspective in Liver Diseases 2016

Early Bird Registration
Until 30 September 2015

Save the date: 20 - 23 January 2016

See you in Chiang Mai, Thailand

NEW PARADIGMS in The Management of Liver Diseases

20-23 January 2016
Khum Kham Convention Complex
Chiang Mai, Thailand
EASL 2015 HCV*: Tx-Naive or PR-Exp’d, GT1, 4, 5, or 6, Without Cirrhosis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>1a</th>
<th>1b</th>
<th>4</th>
<th>5 or 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + PR</td>
<td>12 wks</td>
<td>12 wks</td>
<td>12 wks</td>
<td>12 wks</td>
</tr>
<tr>
<td>SMV + PR</td>
<td>12 wks (naive or relapse) 24 wks (partial/null)</td>
<td>12 wks (naive or relapse) 24 wks (partial/null)</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>8-12 wks,† no RBV</td>
<td>12 wks, no RBV</td>
<td>12 wks, no RBV</td>
<td></td>
</tr>
<tr>
<td>OBV/PTV/RTV + DSV</td>
<td>12 wks, + RBV</td>
<td>12 wks, no RBV</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>OBV/PTV/RTV</td>
<td>Not recommended</td>
<td>12 wks + RBV</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>SOF + SMV</td>
<td>12 wks, no RBV</td>
<td>12 wks, no RBV</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>SOF + DCV</td>
<td>12 wks, no RBV</td>
<td>12 wks, no RBV</td>
<td>12 wks, no RBV</td>
<td></td>
</tr>
</tbody>
</table>

*Recommendations the same for HCV-monoinfected and HCV/HIV-coinfected pts. †8 wks may be used in treatment-naive pts without cirrhosis if baseline HCV RNA < 6 million IU/mL, but should be done with caution, especially in pts with F3 fibrosis.

**EASL 2015 HCV**: Tx-Naive or PR-Exp’d, GT1, 4, 5, or 6, Compensated Cirrhosis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>HCV Genotype 1a</th>
<th>HCV Genotype 1b</th>
<th>HCV Genotype 4</th>
<th>HCV Genotype 5 or 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + PR</td>
<td>12 wks</td>
<td>12 wks</td>
<td>12 wks</td>
<td>12 wks</td>
</tr>
<tr>
<td>SMV + PR</td>
<td>12 wks (naive or relapse)</td>
<td>12 wks (naive or relapse)</td>
<td>24 wks (partial/null)</td>
<td>Not recommended</td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>12 wks + RBV or 24 wks, no RBV or 24 wks + RBV if negative predictors</td>
<td>12 wks + RBV or 24 wks, no RBV or 24 wks + RBV if negative predictors</td>
<td>12 wks + RBV or 24 wks, no RBV or 24 wks + RBV if negative predictors</td>
<td></td>
</tr>
<tr>
<td>OBV/PTV/RTV + DSV</td>
<td>24 wks + RBV</td>
<td>12 wks + RBV</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
<tr>
<td>OBV/PTV/RTV</td>
<td>Not recommended</td>
<td>24 wks + RBV</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>SOF + SMV</td>
<td>12 wks + RBV or 24 wks, no RBV</td>
<td>12 wks + RBV or 24 wks, no RBV</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>SOF + DCV</td>
<td>12 wks + RBV or 24 wks, no RBV</td>
<td>12 wks + RBV or 24 wks, no RBV</td>
<td>12 wks + RBV or 24 wks, no RBV</td>
<td></td>
</tr>
</tbody>
</table>

*Recommendations the same for HCV-monoinfected and HCV/HIV-coinfected pts.

## EASL 2015 HCV*: Tx-Naive & PR-Exp’d, GT2 or 3

<table>
<thead>
<tr>
<th>Regimen</th>
<th>No Cirrhosis</th>
<th>Compensated Cirrhosis (Child-Pugh A)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GT2</td>
<td>GT3</td>
</tr>
<tr>
<td>SOF + PR</td>
<td>12 wks</td>
<td>12 wks</td>
</tr>
<tr>
<td>SOF + RBV†</td>
<td>12 wks</td>
<td>24 wks</td>
</tr>
<tr>
<td>SOF + DCV</td>
<td>12 wks, no RBV</td>
<td>12 wks, no RBV</td>
</tr>
</tbody>
</table>

*Recommendations the same for HCV-monoinfected and HCV/HIV-coinfected pts.
†Best first-line option for genotype 2 HCV; other options may be useful in pts with GT 2 HCV who experience tx failure on sofosbuvir plus ribavirin. Suboptimal for genotype 3 HCV, particularly in pts with cirrhosis and previous failure of PR.