2nd International HIV/Viral Hepatitis Co-Infection Meeting

Friday, July 17 – Saturday, July 18, 2015
Sheraton Wall Centre, Vancouver, Canada

Theme - HIV/Viral Hepatitis: Antiviral Therapy Development and Access

For more information and to register, visit:
coinfectionmeeting.com

PHOTO BY JAMESZ_FLICKR
Highlights from the Meeting

• Only international meeting that brings together all the stakeholders in HIV/Hepatitis Coinfection to work towards equitable access to Hepatitis therapy globally
  – Review latest science
  – Identify barriers
  – Learn from recent successes in low middle and high income countries
  – Engage all partners in constructive solutions
Improved sustained virological response (cure rate) with newer HCV medicines

HCV treatment revolution
2.2% have treatment (WHO 2014)
The urgency of the issue

Annual mortality from the major infectious diseases

- HIV/AIDS
- Viral hepatitis
- Tuberculosis
- Malaria

GBD The Lancet Dec 2012

This is hepatitis...

World Hepatitis Alliance
Change the mindset

• Challenge the prevailing mindset such that viral hepatitis joins HIV, malaria and tuberculosis as the most important infectious diseases

• Funders, government officials, NGOs, medical societies, foundations, man-in-the-street

• Advocacy is key - 240 million people who are chronically infected with HBV (plus 130 million HCV), if only a fraction could be empowered to respond...
Improving the cascade of care

Modeled data for non-VA US population

Yehia PLoS One 2014
Cost of screening can be calculated in different populations

Example: Switzerland

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>General (1924-2013)</th>
<th>40-44 years (1969-1973)</th>
<th>50% of cases (1959-1978)</th>
<th>75% of cases (1949-1983)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence and diagnosis rates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HCV prevalence</td>
<td>1.3%</td>
<td>2.3%</td>
<td>2.2%</td>
<td>2.1%</td>
</tr>
<tr>
<td>HCV RNA prevalence</td>
<td>1.0%</td>
<td>1.8%</td>
<td>1.8%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Diagnosis Rate</td>
<td>40%</td>
<td>40%</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td><strong>Number of tests required to identify 1 viremic case to treat (n)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>158</td>
<td>92</td>
<td>94</td>
<td>101</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Genotype</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Associated costs to identify 1 viremic case, by test type (CHF)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>3,939</td>
<td>2,295</td>
<td>2,357</td>
<td>2,531</td>
</tr>
<tr>
<td>HCV RNA</td>
<td>226</td>
<td>226</td>
<td>226</td>
<td>226</td>
</tr>
<tr>
<td>Genotype</td>
<td>180</td>
<td>180</td>
<td>180</td>
<td>180</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4,345</td>
<td>2,701</td>
<td>2,763</td>
<td>2,937</td>
</tr>
</tbody>
</table>
The favorable safety profiles of new DAA combinations suggest that minimal laboratory monitoring will be necessary to assess safety during treatment.

Diagnostics and monitoring could be limited to:

- two HCV antigen tests to confirm chronic infection before treatment and clearance after treatment (detection limit HCV RNA >2000 IU/mL: US$34 for two tests

- two full blood counts + clinical chemistry tests (ALT / creatinine): US$22

- genotyping if necessary: US$90 (not needed if treatment is pan-genotypic)

HCV Diagnosis Rate, Treatment Rate and Prevalence

# HCV burden among PWID in LMICs

- 10 out of 16 million PWIDs have anti-HCV antibodies \((Nelson, Lancet, 2011)\) → more than 5% of the HCV+ are PWIDs globally
- PWID-HCV+: 26% live in East/SouthEast Asia and 23.5% in Eastern Europe \((Nelson, Lancet, 2011)\)

### PWID-HCV+ in Selected Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of Adults with HCV Antibodies</th>
<th>% of PWIDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>0.14 million</td>
<td>25.6%</td>
</tr>
<tr>
<td>Ukraine</td>
<td>1.1 million</td>
<td>21.5%</td>
</tr>
<tr>
<td>Russia</td>
<td>4.1 million</td>
<td>40.4%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>0.64 million</td>
<td>5.6%</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1.4 million</td>
<td>2.7%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>2.7 million</td>
<td>9.2%</td>
</tr>
</tbody>
</table>

(adapted from Luhmann et al. IJDP. forthcoming)

2nd International HIV/Viral Hepatitis Co-infection Meeting IAS Vancouver 2015
Use of non-sterile equipment needs to be eliminated

Fig 1 Injection equipment soaked in tepid water before reuse in the absence of sterilisation, Africa, 2000. Note the plastic syringes rinsed in the tepid water and the multidose medication vials

Fig 2 Number of injections per person and per year and proportion of these administered with injection equipment reused in the absence of sterilisation, by region, 2000

Potential role of addiction care

Testing, awareness and counseling

Evaluation, retention and adherence

Prevention of reinfection
Increasing treatment and SVR can significantly reduce the number of viremic infections.
Increasing treatment and SVR can significantly reduce the disease burden.
Toranomon Hospital cohort: reduction in HCC incidence with ETV greater among cirrhotic patients

Barriers to HCV treatment

(Wolfe et al. Special issue on HCV and drug use. IJDP. forthcoming)
5g of diamonds
25 1-carat ($1900 each)
Cost = $48,000

5g of daclatasvir
12 weeks of treatment, 60mg/day
Cost = $53,000 (UK price)
Daclatasvir: generic prices

Cost of API = $10,000/kg

API needed per person = 5g (60mg x 84 days)

API per 12 weeks = $50

Formulation = 40%

Formulated drug = $70

Packaging = $0.35/month

Packaged drug = $71

Profit margin = 50%

Final generic Price = $107

For mid 2015, Prices falling rapidly
The ideal DAA treatment: low cost, ≥90% SVR, pan-genotypic, short duration, well tolerated

![Graph showing percent SVR by genotype]

- G1, n≥50: ≥90%
- G2, n≥50: ≥90%
- G3, n≥50: ≥90%
- G4, n≥50: ≥90%
- G5, n≥50: ≥90%
- G6, n≥50: ≥90%
Sofosbuvir + Daclatasvir ± RBV (12 or 24 weeks)

Sources: A1444040 trial; ALLY-1; ALLY-2; ALLY-3; 3 French EAPs
Registration status worldwide of Sovaldi® and Daklinza®

- Countries where Daklinza® is registered:
  - Red

- Countries where Sovaldi® is registered:
  - Teal

- Countries where Daklinza® & Sovaldi® are registered:
  - Stripes

- High income countries:
  - Yellow
BUT G3 Remains a Concern in the Real World
TRIO: 24 Wks SOF + RBV for GT3 HCV in Real-World Settings

- 18 academic and 17 community practices in US TRIO network
  - 24 wks sofosbuvir + RBV (N = 96)
- ITT population: n = 96; PP population (completed therapy with SVR12 data): n = 77
- Key baseline characteristics
  - Male: 56%
  - HCV RNA > 6 x 10^6 IU/mL: 15%
  - Cirrhosis: 30%
  - Previously treated: 39%
- 2/96 pts died from causes not related to treatment

Selection of RAVs in Patients who Failed after LDV (no SOF)

Patients who failed after a ledipasvir-containing treatment (without sofosbuvir)

Before LDV Treatment

- 84% (64/76) Patients without NS5A RAVs
- 16% (12/76) Patients with NS5A RAVs

At Virologic Failure With LDV Treatment

- 99% (72/73) Patients without NS5A RAVs
- 1% (1/73) Patients with NS5A RAVs

(Dvory-Sobol et al., EASL 2015)
The NS5A RAVs are Persistent
24 Wks LDV/SOF After Failure of LDV/SOF-Based Therapy: Effect of Baseline RAVs


<table>
<thead>
<tr>
<th>SVR12 by Baseline NS5A RAVs, n/N (%)</th>
<th>LDV/SOF for 24 Wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of RAVs</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11/11 (100)</td>
</tr>
<tr>
<td>1</td>
<td>11/16 (69)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>7/14 (50)</td>
</tr>
<tr>
<td>Single NS5A RAV</td>
<td></td>
</tr>
<tr>
<td>Q30R or M28T</td>
<td>5/5 (100)</td>
</tr>
<tr>
<td>L31M</td>
<td>4/5 (80)</td>
</tr>
<tr>
<td>Y93H/N</td>
<td>2/6 (33)</td>
</tr>
</tbody>
</table>

- NS5B variants emerged during retreatment in 33% of pts (4/12) with virologic failure
  - **S282T**: n = 2; **L159F**: n = 1; **S282T + L159F**: n = 1
Treatment volumes increasing

Make sure you have the capacity to treat & follow everyone
Clinic Issues

• Matching needs of your population
  – Setting (hospital vs clinic vs the street)
  – Support services (social work, addiction counseling)

• Triage
  – Who gets treated first?

• Paper work
  – Without systems in place…you will drown!

• Following patients on treatment
  – Capacity (MD/RN/other), frequency, liver disease
HCV in Mongolia

- Genotype 1b (98%)
- Anti-HCV average 9.8-15% (285,700-450,000 people)
  - Elder people up to 33%
  - Health workers >50% co-infected HCV and HBV
  - 82% reported needle-stick injuries in 2008
- Viremic 6.8-11% (210,000-330,000 people)
- Diagnosed ever: 60,000 (1300 new diagnoses 2013)
  - Liver biopsy: 40-60/year (mainly for HCC); Fibroscans: >3000
- Treated (PEG/RBV): 200; DAAs: happy few
- Liver transplants: 8 (of which 3 due to HCV)
- LC >>350/100,000 many undiagnosed
- 15% of all mortality due to LC/HCC (2\textsuperscript{nd} cause of death, esp. in 40-65 age group)
- HCC mortality: 63.2/100,000; world record, 8x world average

18/07/2015 Mongolia - how to stop the HCV epidemic?
Mongolia - latest actions

• New guidelines for treatment of HCV approved
• 100 “Hep-C frontline” doctors trained (in capital & 21 provinces)
  » SOF + LDP roll-out expected Nov 2015 ($400/month)
  » Generic tenofovir now available $25/m for HBV+ pregnant women
• Dialogue on financing options for hepatitis care & treatment
  » Standard package of services for hep C and B?
  » Economic analysis of hep C and B care and treatment
• Discussing new National programme on viral hepatitis (not only HCV)
• Website to link providers, patients, labs and the NCCD for hepatitis screening, care and treatment patients.
• **Team building & teamwork**
  
  – Ministry of Health  
  Brazilian Health Surveillance Agency (Anvisa)  
  Secretariat of Health Surveillance (SVS/MS)  
  Secretariat of Science, Technology and Strategic Inputs (SCTIE/MS)  
  – Organized Civil Society,  
  – Healthcare providers

**GOAL**

**TREAT 60,000 PEOPLE IN THE NEXT TWO YEARS.**
Perspectives July 2015 Onward

Sustained Virological Response (SVR)

- INTERFERON-FREE
  - SOF+DAC/SIM (2015-)
  - >90%
  - F3/F4 (F2), HIV, Pr/P Tx...
  - 30,000

  - 40%
  - 15,000

Treatments/year

Population with Treatment Recommended
What needs to happen?

1. New funding for HCV treatment to be established at either national or international level, to allow large drug orders to be made, and these economies of scale to be achieved.

2. Clear and transparent treatment access policies with voluntary licensing, from all companies making DAAs (BMS, Merck, AbbVie).

3. Feasibility studies of DAA combinations in LMICs to prove this can be done cheaply.

4. Low cost point of care tests to monitor viral load or antigen.
In the next 25 years, HCV can be eliminated

Today

Future

New HCV Infections

Cured

Mortality

New HCV Infections

Cured

Mortality
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#ACureForAll

WIFI PASSWORD : trails15

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