A Nation-wide Investigation of Real-World Community Effectiveness in HCV Treatment for Policy-making Toward Elimination of HCV by 2030 in Taiwan

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Conflicts of Interest

• Research support from Abbvie, Abbott, BMS, Gilead, Merck and Roche.

• Consultant of Abbvie, Abbott, Ascletis, BMS, Gilead, J&J, Merck, Novartis, Pharmaessential and Roche.

• Speaker of Abbvie, Abbott, Ascletis, BMS, Gilead, Merck, Pharmaessential and Roche.
BACKGROUND

• Hepatitis C virus (HCV) treatment has emerged from interferon (IFN)-based to IFN-free direct acting antivirals (DAA) therapy since 2014.

• To achieve the goal of HCV elimination by 2030 set by WHO, we conducted serial nation-wide investigations for policy-making to eliminate HCV in Taiwan, an HCV hyperendemic area.

METHODS

- Where we are in HCV control?
- What cost it is worth to cure a patient?
- How it can be done to eliminate HCV?
Constructing a model to evaluate the rates of disease diagnosis, awareness, accessibility, treatment rate, and clinical efficacy of HCV at national level.

**Age, sex-adjusted HCV prevalence in Taiwan**
- anti-HCV 3.3%
  - 745,000
- HCV viremics (74.5%)
  - 554,000

**Successful treatment rate with PegIFN/RBV in Taiwan**
- HCV-1 (N=528)
  - SVR: 80%
  - 16.90% relapsers
  - 3.10% non-responders
- HCV-2 (N=482)
  - 74% SVR
  - 89%

HCV genotype 1 vs. 2:
Distribution: 50% vs. 45%

Constructing a model to evaluate the rates of disease diagnosis, awareness, accessibility, treatment rate, and clinical efficacy of HCV at national level.

A Huge Gap between clinical efficacy and community effectiveness (2012)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rate (est. number, 1000 persons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HCV prevalence</td>
<td>745</td>
</tr>
<tr>
<td>Correct diagnosis</td>
<td>745</td>
</tr>
<tr>
<td>HCV viremic</td>
<td>554</td>
</tr>
<tr>
<td>Disease awareness</td>
<td>270</td>
</tr>
<tr>
<td>Access</td>
<td>107</td>
</tr>
<tr>
<td>Recommendation</td>
<td>75</td>
</tr>
<tr>
<td>Clinical efficacy (80%)</td>
<td>60</td>
</tr>
</tbody>
</table>

HCV viremics

- 100%
- 100%
- 48.7%
- 19.2%
- 13.7%
- 10.9%

Causes for not being treated for HCV in Clinics

- Fear of adverse effects: 36.93%
- Ineligibility: 17.63%
- Therapy unawareness: 11.31%
- Ineligibility for insurance reimbursement: 17.55%
- Hematological disorders: 6.98%
- Major psychiatric problems: 2.57%
- Major systemic diseases: 8.08%

To achieve the goal of HCV elimination by 2030, we have to increase the rates of disease diagnosis, awareness, accessibility and introduce antiviral regimens with high cure rates and safety profiles.

Where we are in HCV control?

What cost it is worth to cure a patient?

How it can be done to eliminate HCV?

IFN-free DAA regimens for HCV Therapy

<table>
<thead>
<tr>
<th>Higher</th>
<th>Simpler</th>
<th>Shorter</th>
<th>Safer</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV</td>
<td>ASV</td>
<td>24w</td>
<td>G1b</td>
</tr>
<tr>
<td>PTVr</td>
<td>OBV</td>
<td>12w</td>
<td>G1/4</td>
</tr>
<tr>
<td>GZR</td>
<td>EBR</td>
<td>12/16w</td>
<td>G1/4</td>
</tr>
<tr>
<td>SOF</td>
<td>LDV</td>
<td>8/12w</td>
<td>G1-6</td>
</tr>
<tr>
<td>SOF</td>
<td>DCV</td>
<td>12w</td>
<td>G1-4</td>
</tr>
<tr>
<td>SOF</td>
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<td>12w</td>
<td>G1/4</td>
</tr>
<tr>
<td>SOF</td>
<td>VEL</td>
<td>12w</td>
<td>G1-6</td>
</tr>
<tr>
<td>SOF</td>
<td>VEL</td>
<td>12w</td>
<td>G1-6</td>
</tr>
<tr>
<td>GLE</td>
<td>PIB</td>
<td>8/12w</td>
<td>G1-6</td>
</tr>
</tbody>
</table>

Barriers to Treatment in DAA era

- **11K-80K USD/SVR**
  - Huge budget impact
- Warehouse patient pool
  - Impact on professional manpower
- Cost-effectiveness of DAA
- Prioritization of DAA Treatment

DCV, daclatasvir; ASV, asunaprevir; PTVr, paritaprevir/ritonavir; OBV, ombitasvir; DSV, dasabuvir; GZR, grazoprevir; EBR, elbasvir; SOF, sofosbuvir; LDV, ledipasvir; SIM, simprenvir; VEL, velpatasvir; VOX, voxilaprevir; GLE, glecaprevir; PIB, pibrentasvir
Evaluating the cost-effectiveness of Peg-IFN/RBV for HCV by linking a real world cohort to the National Health Insurance database as a reference of DAA cost for policy-makers.

- 1,926 HCV patients with PegIFN/RBV therapy
- Linking well characterized clinical features to big data from National Health Insurance Research Database (NHIRD) of Taiwan
- Total cost of outpatient & inpatient: antivirals, non-antivirals medicine, intervention, lab, consultation, and logistic costs

<table>
<thead>
<tr>
<th>Cost (USD) per SVR</th>
<th>Naïve (N=1,809)</th>
<th>Experienced (N=117)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Genotype 1</td>
<td>$8,285 ± 4,032 (n=829)</td>
<td>$15,520 ± 5,915 (n=82)</td>
</tr>
<tr>
<td>HCV Genotype 2</td>
<td>$4,663 ± 3,382 (n=980)</td>
<td>$10,324 ± 4,742 (n=35)</td>
</tr>
</tbody>
</table>

- The adjusted price is **$8,050 USD** per successful treatment with PegIFN/RBV for treatment naïve and experienced HCV patients

Where we are in HCV control? $ What cost it is worth to cure a patient? How it can be done to eliminate HCV?

Risk of liver cancer and liver fibrosis status

- **F0-1 (n=592)**
  - Low risk of HCC in F0-F1 patients irrespective of SVR status

- **F2-4 (n=689)**
  - Risk of HCC significantly reduced in F2-F4 patients achieving an SVR

Risk of liver cancer and patient age

- **Age < 40 years (n=216)**
  - Adjusted p value <0.0001
  - Non-SVR vs. SVR: Adjusted HR(CI), 4.91 (2.42-9.97)

- **Age ≥ 40 years (n=1,065)**
  - Adjusted p value <0.0001
  - Non-SVR vs. SVR: Adjusted HR(CI), 2.76 (0.41-18.84)

The data highlighted the urgency of successful treatment for aged patients and/or for patients with advanced liver fibrosis.

Where we are in HCV control?

What cost it is worth to cure a patient?

How it can be done to eliminate HCV?

**National Hepatitis C Program (NHCP) Office set in Taiwan, 2016**

- **Co-conveners**
  - Minister of Health and Welfare: Academician Ding-Shih-Chen
  - Vice Convener: Vice Minister of Health and Welfare

**Task Group**
- Minister of Science and Technology
- Academiaer M. F. Chen
- Academiaer W. H. Chang
- Professor W. N. Chang

**Where we are in HCV control?**

- What cost it is worth to cure a patient?
- How it can be done to eliminate HCV?

**Strategies toward HCV Elimination at National Level**

- Prevent new HCV infection
  - with universal educational programs for general population & health-care providers by NGO/GO

**Education decreased anti-HCV prevalence in HCV-hyperendemic areas of southern Taiwan**

<table>
<thead>
<tr>
<th></th>
<th>Adult population</th>
<th>Teenage population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence (%)</td>
<td>Prevalence (%)</td>
</tr>
<tr>
<td>1993-4</td>
<td>4.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>1997-2005</td>
<td>0.7%</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

Education decreased anti-HCV prevalence in HCV-hyperendemic areas of southern Taiwan.

Where we are in HCV control?

What cost it is worth to cure a patient?

How it can be done to eliminate HCV?

National Hepatitis C Program (NHCP) Office set in Taiwan, 2016

**Strategies toward HCV Elimination at National Level**

- **Prevent new HCV infection**
  - With universal educational programs for general population & health-care providers by NGO/GO
- **Increase rates of diagnosis/awareness**
  - With multi-proposed, integrated programs of community survey by NGO
  - With free check-up of HBV and HCV markers for adults with age > 45 years by GO
- **Increase accessibility**
  - Provide “point-of-care” service with specialized professionals in rural areas
- **Scale-up treatment uptake**
  - With reimbursement of DAA regimens at a fixed price of 8,300 USD per SVR achieved by Taiwan National Health Insurance, whatever DAA regimens
  - Prioritizing treatment by prior treatment experience and liver fibrosis status of HCV patients

Yu-10
DAA reimbursement for HCV in Taiwan, 2017

- **Budget:** 75 million USD
  - BMS, DCV + ASV
  - Abbvie, PrOD (3 DAA)
  - Merke, GZR/EBR
- **Target population:**
  - 9,000 patients
  - HCV genotype 1 or 1a or 1b
  - Fibrosis score 3 or 4
  - Treatment naïve or experienced

- **Enrollment:** completed in September
- **Efficacy:** (assessed in August, 2017)
  - **99.2%** (941/949, among 1009 patients with post treatment week 12 HCV RNA data available)

DAA reimbursement for HCV in Taiwan, 2018

- **Budget:** **140** million USD
  - BMS, DCV + ASV
  - Abbvie, PrOD (3 DAA)
  - Merke, GZR/EBR
  - **Gilead, SOF + RBV, SOF/LDV**
- **Target population:**
  - 20,000 patients
  - HCV all genotypes
  - Fibrosis score 3 or 4
  - Treatment naïve or experienced
Conclusions

• The key issue to achieve the goals of WHO in HCV elimination by 2030 is to increase the rate of disease diagnosis, awareness, accessibility and financing.

• The results from our serial nation-wide investigations could provide evidence and references for policy-making to achieve HCV elimination at national level.
Where we are in HCV control?

What cost it is worth to cure a patient?

How it can be done to eliminate HCV?

• HCC is the most risky complication of HCV
• Factors associated with HCC risk after SVR

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Age</td>
</tr>
<tr>
<td>DM</td>
<td>Hepatic fibrosis</td>
</tr>
<tr>
<td>rGT levels</td>
<td>ALT-M6</td>
</tr>
<tr>
<td>AFP levels</td>
<td>APRI-M6</td>
</tr>
</tbody>
</table>

Factors unchangeable or fluctuated

Factors worsening with time

- Time-degenerative factors

Prioritizing HCV Treatment with Time-degenerative factors

• 1,281 chronic hepatitis C subjects with pretreatment biopsy and treated with PegIFN/RBV in KMUH
• Linking to National Cancer Registry
• Comparing the risk of HCC between patients with and without successful viral eradication among different subgroups