Will HCV therapies deliver global impact?

Professor Greg Dore
Disclosures

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• Gregory Dore has served on advisory boards for Gilead, Bristol Myers Squibb, Abbvie, Merck, and Janssen;
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The global burden of chronic HCV infection is enormous and escalating, with limited impact of HCV treatment.
Global chronic HCV prevalence

Prevalence (Viremic)   Total Infected (Viremic)
0.0%-0.6%             0-200K
0.6%-0.8%             200K-650K
0.8%-1.3%             650K-1.9M
1.3%-2.9%             1.9M-3.5M
2.9%-7.8%             3.5M-9.2M
Global chronic HCV prevalence

![Graph showing the total viremic infections, all ages (millions) for various countries. The countries with the highest prevalence include China, Pakistan, Nigeria, Egypt, and India.](image-url)
Global HCV treatment uptake: pre-IFN free DAA
Global deaths from end-stage liver disease

Deaths due to HCV more than doubled between 1990–2013; HCC deaths due to HCV increased 300%
Chronic HCV liver disease burden

Estimates and projections of Decomp Cirrhosis and HCC in Australia
The development of interferon-free HCV therapy provides one of the major advances in clinical medicine in recent decades
IFN-free DAA therapy: OST vs non-OST

GT1, treatment naïve, F0-4; 12 weeks duration

IFN-free DAA therapy: HCV vs HIV/HCV

GT1, treatment naïve, F0-4; 12 weeks duration

Afdhal, NEJM2014; Naggie, CROI2015; Feld, NEJM2014; Rockstroh, WAC2014; Wyles, CROI2015; Zeuzem, ILC2015; Rockstroh, ILC2015; Poordad, ILC2015
IFN-free DAA therapy

Patient reported outcomes during and following treatment

PRO Measurement Scale
- NORMALIZED TOTAL FACIT-F
- NORMALIZED FACIT-FS

Younossi ZM, AASLD 2014, #77 (Courtesy Ed Gane)
Global HCV genotype distribution

Gower E et al. J Hepatol 2014
Sofosbuvir/Velpatasvir

GT1-6, treatment naïve and exp. (28%), F0-4 (21% F4), 12 wks

SVR12 %

<table>
<thead>
<tr>
<th>GT</th>
<th>SVR12</th>
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<tbody>
<tr>
<td>GT1</td>
<td>323/328</td>
</tr>
<tr>
<td>GT2</td>
<td>237/238</td>
</tr>
<tr>
<td>GT3</td>
<td>264/277</td>
</tr>
<tr>
<td>GT4</td>
<td>116/116</td>
</tr>
<tr>
<td>GT5</td>
<td>34/35</td>
</tr>
<tr>
<td>GT6</td>
<td>41/41</td>
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Gilead press release, 21 Sep 2015
Interferon-free HCV therapy drug pricing is a major impediment to global impact
HCV treatment pricing: 12 week regimens (US)

$US 1,000

- SOF/SIM
- SOF/LED
- PTV/OBV/DSV
- GZV/ELB

Legend:
- Listed
- Discounted
Sofosbuvir Medicaid restrictions in US

Liver disease stage

Map showing the distribution of METAVIR fibrosis stages across the United States.
HCV treatment: minimum costs

$US

- Monitoring
- Genotype
- Treatment

- SOF/RBV (24 wk)
- SOF/LED (12 wk)
- SOF/DCV (12 wk)
- GZV/ELB (12 wk)
HCV treatment: drug price reform

Strategies

• Pharmaceutical industry competition

• Discounting, risk-sharing arrangements, volume taxation

• Voluntary licenses (Gilead + Generic companies in 101 LMICs)

• Compulsory licenses

• Advocacy/Activism
Australian PBAC approach

• Independent body that advises Australian Government

• Recommended that all people with chronic HCV be eligible

• Probable price per course (8, 12, or 24 weeks)

• Required cost-effectiveness $15,000/ICER

• Probable treatment cap: 60,000 over 5 years

• Treatment provided above cap at reduced or no profit

• Ongoing price negotiations and Federal Cabinet approval required
There are multiple barriers to HCV treatment among PWID
Global harm reduction strategies

Only 41% (n=82) of countries had implemented NSPs

Only 35% (n=70) of countries had implemented OST

Sofosbuvir Medicaid restrictions in US

Illicit drug use

Sofosbuvir Medicaid restrictions in US

AASLD/IDSA HCV treatment guidelines

“Recent and active IDU should not be seen as an absolute contraindication to HCV therapy.”

“Scale up of HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the United States and globally.”
The broad implementation of interferon-free HCV therapy has the potential to markedly reduce disease burden.

Australia should be in an unique position to address the burden of HCV disease, if PBAC recommendations are approved.
HCV treatment and care cascade in Australia

- **Living with chronic HCV infection**: 230,470
- **Diagnosed living with chronic HCV infection**: 172,720
- **Ever received HCV treatment**: 45,000
- **HCV cured**: 24,755

- **75% Diagnosed**
- **20% Treated**
- **11% Cured**
PBAC recommendations: March, July 2015

- Sofosbuvir + Ledipasvir for GT1
- Sofosbuvir + Daclatasvir for GT1 and 3
- Sofosbuvir + Ribavirin for GT2
- Sofosbuvir + PEG-IFN/RBV for GT1
- Paritaprevir/r + Ombitasvir + Dasabavir (+/- RBV) for GT1
- No liver disease stage or drug use restrictions
- General practitioner prescribing and community pharmacy dispensing
Impact of HCV treatment on disease burden

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Graph</th>
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<tbody>
<tr>
<td>Base case</td>
<td><img src="image" alt="Base case graph" /></td>
</tr>
<tr>
<td>Increase SVR with no increase in annual treated population and no fibrosis-restricted eligibility</td>
<td><img src="image" alt="Increase SVR base case graph" /></td>
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<tr>
<td>Increase SVR and annual treated population</td>
<td><img src="image" alt="Increase SVR population graph" /></td>
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<tr>
<td>Increase SVR and annual treated population restricted to ≥F3 (2015–2017) then unrestricted (all ≥ F0) from 2018</td>
<td><img src="image" alt="Increase SVR and annual treated population restricted graph" /></td>
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</tbody>
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*Note: The figures represent different scenarios of HCV treatment impact on disease burden, including the number of infected cases, cirrhosis, HCC, and liver-related deaths.*

HCV treatment uptake in United States

Chronic HCV = 3,400,000

* Extrapolated

5%
HCV treatment uptake in Spain

Chronic HCV = 473,000

* Extrapolated

CDA 2015: Polaris Observatory (http://centerforda.com/polaris/)
The way forward

- Global leadership (UN, WHO, partner orgs, Country champions)
- Massive increase in HCV screening
- Linkage to treatment and care
- Utilisation of HIV and harm reduction frameworks
- Simplified HCV treatment monitoring
- Enhanced epidemiological and evaluation capacity
- Civil society involvement
Positive international HCV developments

- WHA resolution 63.18: Viral Hepatitis Global Public Health Priority (2010)
- WHA resolution 67.6: Enhanced call for Member State action (May 2014)
- WHO release 1st International HCV Treatment Guidelines (April 2014)
- Global Fund for AIDS, TB and Malaria include HCV treatment (March 2015)
- WHO add new DAAS including sofosbuvir to Essential Medicines List (2015)
- WHO 2030 HCV targets: 90% incidence and 65% mortality decline; 80% treat
- World Hepatitis Summit (September 2015)
HCV diagnosis and treatment uptake

Bubble Area: Viremic HCV Prevalence

Treatment Rate (%)

Diagnosis Rate (%)
Simplified HCV treatment monitoring

Diagnosis/monitoring

- Point of care (PoC) HCV diagnosis
- HCV core antigen (whole blood)
- HCV RNA (dried blood spot)
- Simplified disease staging
- Limited treatment monitoring (SVR12 only?)
- No post-treatment HCC surveillance

Decentralised
Advocacy and Activism

hep Coalition

TAG
Treatment Action Group

INPUD
International Network of People who Use Drugs

AIDS ACCESS FOUNDATION

I - MAK
Initiative for Medicines, Access & Knowledge

ITPC

Working Group of Intellectual Property

ACCESS®
HCV Treatment

http://www.hepcoalition.org
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