Hepatitis C: The Treatment Landscape in 2017

On the road to HCV elimination?

Professor Greg Dore

Disclosures

Funding and speaker fees from AbbVie, Bristol-Myers Squibb, Gilead Sciences and Merck
HCV Treatment in 2017

- Overview of DAA uptake in 2016 and early 2017
- Patterns of DAA treatment, including prescriber type
- HCV treatment among sub-populations: cirrhosis and PWID
- HCV elimination modelling
- DAA treatment outcomes: REACH-C study
- Strategies to continue DAA uptake

Evolution of HCV therapies

Adapted from Dore G, Feld JJ. Clin Infect Dis 2015;60:1829–36

<table>
<thead>
<tr>
<th>Tolerability</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>48 weeks</td>
<td>PEG-IFN + RBV + SMV</td>
</tr>
<tr>
<td>24–48 weeks</td>
<td>SOF + RBV</td>
</tr>
<tr>
<td>24 weeks</td>
<td>PEG-IFN + TVR</td>
</tr>
<tr>
<td>12 weeks</td>
<td>PEG-IFN + RBV</td>
</tr>
<tr>
<td></td>
<td>IFN</td>
</tr>
</tbody>
</table>

BOC: boceprevir; DCV: daclatasvir; DSV: dasabuvir; EBR: elbasvir; GZR: grazoprevir; LDV: ledipasvir; OMV: ombitasvir; PEG-IFN: pegylated interferon; PTV: paritaprevir; RBV: ribavirin; RTV: ritonavir; SMV: simeprevir; SOF: sofosbuvir; TVR: telaprevir
Evolution of HCV therapies

Adapted from Dore G, Feld JJ. Clin Infect Dis 2015;60:1829–36

Australian Government-funded DAAs

Gilead Sciences, SOVALDI Australian PI, March 2015; Gilead Sciences, HARVONI Australian PI, June 2016; Bristol-Myers Squibb, DAKLINZA Australian PI, August 2016; AbbVie; VIEKIRA PAK-RBV PI, August 2016, Merck Sharp & Dohme, ZAPATIER ARTG August 2016; Gilead Sciences, EPCLUSA Australian PI August 2017
Australia has prepared the foundation for elimination of HCV as a major public health issue, by 2026-2030

HCV care cascade in Australia: end 2015

HCV treatment in Australia

- DAA therapy for all Australians ≥18 years with chronic HCV
- No liver disease stage, or drug and alcohol restrictions
- Broad practitioner base (including GPs) with public hospital (S100) and community pharmacy (S85) dispensing

<table>
<thead>
<tr>
<th>Date listed</th>
<th>Generic name</th>
<th>Genotype</th>
<th>Duration (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2016</td>
<td>Sofosbuvir/Ledipasvir</td>
<td>1</td>
<td>8-24</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir + Daclatasvir</td>
<td>1, 3</td>
<td>12-24</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir + Ribavirin</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir + Peg-IFN + Ribavirin</td>
<td>1, 3, 4-6</td>
<td>12</td>
</tr>
<tr>
<td>May 2016</td>
<td>Paritaprevir/Ritonavir/Ombitasvir + Dasabuvir +/− Ribavirir</td>
<td>1</td>
<td>12-24</td>
</tr>
<tr>
<td>Jan 2017</td>
<td>Grazoprevir/Elbasvir</td>
<td>1, 4</td>
<td>12-16</td>
</tr>
<tr>
<td>August 2017</td>
<td>Sofosbuvir/Velpatasvir</td>
<td>1-6</td>
<td>12</td>
</tr>
</tbody>
</table>

HCV treatment in Australia

IFN-based vs. IFN-free

32,550 =14% chronic HCV

HCV treatment in Australia: DAA duration

Kirby Institute 2016 (http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)

HCV treatment in Australia: Age distribution

Dotted line represent the age distribution among people living with chronic HCV in 2015 in Australia
DAA treatment uptake is encouraging in key populations for HCV elimination goals: people with cirrhosis and people who inject drugs
**HCV treatment in Australia: Cirrhosis DAA uptake**

![Graph showing HCV treatment uptake by stage and treatment type](image)

- **Not-treated**
- **PBS (2016)**
- **Generic (2015)**
- **Clinical Trials (2014-15)**
- **Early access program (2014-15)**

Early access program (n=1,930): 95% F4; 5% F0-F3
Clinical Trial (n=911): 25% F4; 75% F0-F3
Generic (n=1,500): 30% F4; 70% F0-F3 [Freeman EASL 2016]
PBS (n=32,400): 36% F4; 64% F0-F3

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**HCV treatment uptake: current PWID (ANSPS)**

**Recent and ever HCV treatment uptake 2012 to 2016***

![Graph showing recent and ever HCV treatment uptake](image)

- **Ever (lifetime history)**
- **Recent (last 12 months)**

* Among HCV antibody positive respondents who did not self-report spontaneous clearance
** Respondents with prior treatment-induced clearance were excluded when assessing recent treatment uptake
*** 2012-2016 p-trend<0.001

Iversen J, et al. AVHEC 2017
DAA treatment outcomes are encouraging, but enhanced efforts are required to improve post-treatment follow-up
Real world efficacy of DAAs

**REACH-C**
- Observation cohort from a national network of diverse clinics
- March to December 2016, 1618 patients initiated treatment

<table>
<thead>
<tr>
<th>Clinic</th>
<th>Patients</th>
<th>Location</th>
<th>Type of service/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cairns and Hinterland HHS</td>
<td>608</td>
<td>Cairns, QLD</td>
<td>Tertiary, sexual health, outreach specialist, drug and alcohol, prison</td>
</tr>
<tr>
<td>Kirketon Road Centre</td>
<td>111</td>
<td>Sydney, NSW</td>
<td>Primary care</td>
</tr>
<tr>
<td>Langton Centre</td>
<td>34</td>
<td>Sydney, NSW</td>
<td>Drug and alcohol</td>
</tr>
<tr>
<td>Matthew Talbot Hostel</td>
<td>10</td>
<td>Sydney, NSW</td>
<td>Primary care</td>
</tr>
<tr>
<td>Prince St Medical Centre</td>
<td>82</td>
<td>Orange, NSW</td>
<td>General practice</td>
</tr>
<tr>
<td>Royal Adelaide Hospital</td>
<td>113</td>
<td>Adelaide, SA</td>
<td>Tertiary</td>
</tr>
<tr>
<td>Scope Gastroenterology</td>
<td>171</td>
<td>Melbourne, VIC</td>
<td>Private specialist practice</td>
</tr>
<tr>
<td>St Vincent’s Hospital</td>
<td>426</td>
<td>Sydney, NSW</td>
<td>Tertiary, drug and alcohol</td>
</tr>
<tr>
<td>The Byrne Surgery</td>
<td>28</td>
<td>Sydney, NSW</td>
<td>General practice</td>
</tr>
<tr>
<td>Toormina Medical Centre</td>
<td>34</td>
<td>Coffs Harbour, NSW</td>
<td>General practice</td>
</tr>
</tbody>
</table>

Baseline characteristics

- ≥50 years old: 56%
- Male: 70%
- HIV Positive: 8%
- Cirrhosis: 19%
- Injecting drug use in past 6 months: 15%
- Current OST: 19%

HCV Genotype

- Genotype 1a: 57%
- Genotype 1b: 37%
- Genotype 2a: 1%
- Genotype 3a: 1%
- Other: 1%
- Unknown: 4%
Real world efficacy of DAAs

Overall treatment outcomes

Treatment commenced
n=18148

Expected SVR12 by 31 Mar 2017
n=1435

Lost to follow-up (n=45)
Death (n=5)
Unknown SVR (n=216)

SVR
n=1126
Intention to treat: 79.5%
Per protocol: 96.5%

No SVR
n=309
Virological failure (n=18)
Reinfection (n=10)
Other (n=2)
Unknown reason (n=21)

SVR12: sustained virological response 12 weeks after treatment; ITT: intention to treat; PP: per protocol

Real world efficacy of DAAs

SVR12 rates by genotype

per protocol analysis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>SVR12 Rate</th>
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</thead>
<tbody>
<tr>
<td>1a</td>
<td>97.5%</td>
</tr>
<tr>
<td>1b</td>
<td>97.1%</td>
</tr>
<tr>
<td>2</td>
<td>96.4%</td>
</tr>
<tr>
<td>3</td>
<td>94.9%</td>
</tr>
<tr>
<td>4</td>
<td>77.8%</td>
</tr>
<tr>
<td>Other</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotype</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>553</td>
</tr>
<tr>
<td>1b</td>
<td>102</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
</tr>
<tr>
<td>3</td>
<td>393</td>
</tr>
<tr>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>46</td>
</tr>
</tbody>
</table>
Real world efficacy of DAAs

SVR12 rates by clinical characteristics

per protocol analysis

Real world efficacy of DAAs

Missing SVR12 by clinical characteristics

IDU: injecting drug use; OST: opioid substitution therapy
Diverse models of care and DAA access settings are crucial for continued treatment uptake
HCV treatment uptake: 2015-2016

% of chronic HCV

CDA 2017: Polaris Observatory (http://centerforda.com/polaris/)

CDA 2017: Polaris Observatory (http://centerforda.com/polaris/)
HCV treatment in Australia: Prescriber type

Kirby Institute 2017 (http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)

HCV treatment in Australia: 2016

Total: 32,400

Kirby Institute 2017 (http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)
DAA initiations in community pharm. (3,500; >60%)

Data Source: QuintilesIMS and NostraData

DAA prescriptions (total) per month: PBS

Data Source: Prospection
### Key points regarding DAA uptake

- 2016 was always going to be a bumper year, given the broad eligibility and “warehouse” effect

- DAA uptake in 2017 will clearly be lower than 2016, but unclear how much lower: may be less than 25,000

- HCV elimination by 2030 will require sustained DAA uptake, at around 20,000/year

- Need for community awareness campaigns to sustain momentum

- Need for continued funding for community-based organisations

- Need for enhanced monitoring and evaluation

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### Modelling HCV Elimination in Australia

- **Annual number of people receiving HCV treatment**

<table>
<thead>
<tr>
<th>Treatment Scenario</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Post-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pessimistic</td>
<td>7,296</td>
<td>32,400</td>
<td>18,510</td>
<td>13,890</td>
<td>13,890</td>
</tr>
<tr>
<td>Intermediate</td>
<td>7,296</td>
<td>32,400</td>
<td>27,770</td>
<td>23,143</td>
<td>18,510</td>
</tr>
<tr>
<td>Optimistic</td>
<td>7,296</td>
<td>32,400</td>
<td>32,400</td>
<td>32,400</td>
<td>32,400</td>
</tr>
</tbody>
</table>

- Scenarios for each jurisdiction have same relative change in number treated over time starting from the 2016 PBS estimate

- **Status quo : Pre-DAA era scenario**
  - Number on treatment kept at 2015 levels

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Kwon A, et al. AVHEC 2017
Estimated year Australia meets World Health Organization target compared to 2015 estimates

<table>
<thead>
<tr>
<th>Treatment scenario</th>
<th>WHO target</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% reduction in new chronic infections</td>
<td>2028</td>
</tr>
<tr>
<td>80% of people living with chronic HCV treated</td>
<td>2031</td>
</tr>
<tr>
<td>65% reduction in HCV-related deaths</td>
<td>2029</td>
</tr>
</tbody>
</table>

Scenario:
- Pre-DAA PBS listing
- Pessimistic scale-up
- Intermediate scale-up
- Optimistic scale-up
Key high-risk populations will need to be the focus, if HCV elimination to be achieved within next decade

High risk populations for HCV: Australia

- **Current PWID**
  - N=95,000
  - Chronic HCV 40%
  - N=38,000

- **MSM with HIV**
  - N=21,000
  - Chronic HCV 10%
  - N=2,100

- **Prisoners**
  - N=50,000
  - Chronic HCV 25%
  - N=12,500

- **PWID on OST**
  - N=48,000
  - Chronic HCV 50%
  - N=24,000

Larney S, IJDP 2017; Kirby Institute 2017
Monitoring and Evaluation of HCV Elimination

- **DAA scale-up**: Monitoring of DAA uptake, prescriber patterns, geographical coverage, treatment completion, and retreatment

- **Real-world DAA treatment outcomes**: REACH-C/OPERA-C

- **Liver Disease burden**: Data linkage (several jurisdictions) with hospitalisation (DC, HCC), cancer registry (HCC), death registry (liver disease and all-cause mortality), PBS (DAAs), and MBS (procedures).

- **Chronic HCV prevalence in high-risk populations**: ANSPS for current PWID (including DAA resistance monitoring); CEASE/Co-EC for HIV/HCV.

- **HCV transmission: HCV incidence**: ACCESS database; HCV notifications (acute, younger age); **HCV reinfection**: ANSPS, cohort studies in community and prison settings; ACCESS

Conclusions

- Australia is a leading country in relation to initial DAA roll-out, despite a delayed start

- Key populations for HCV elimination are being reached

- A broadened range of models and prescribers should provide sustained momentum, albeit at lower levels than 2016

- DAA outcomes are favourable, although post-treatment follow-up not optimal

- The next 2-3 years are absolutely crucial
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Ms. Tracy Swan (USA)
Dr. Philip Bruggmann (Switzerland)
Prof. Olav Dalgard (Norway)
Prof. Julie Bruneau (Canada)
Dr. Jordan Feld (Canada)