DAA Therapy and Reinfection Among People who Inject Drugs: Forming a Foundation for HCV Elimination

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HCV DAA therapy, reinfection, and elimination among PWID

- DAA therapy is safe and effective among PWID, even in the “real-world”
- We need to acknowledge and accept that HCV reinfection will occur
- Testing, diagnosis, and linkage to care will be a major barrier moving forward
- Simplification of models of care and interventions will be crucial to achieve HCV elimination among PWID
- Remaining challenges for HCV elimination in PWID
DAA therapy is safe and effective among PWID, even in the “real-world”
Defining populations of PWID

- Former PWID
- Current PWID
- Current PWUD
- PWID in OST
People receiving OST – phase II/III trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SVR12 (%)</th>
<th>OST</th>
<th>no OST</th>
</tr>
</thead>
<tbody>
<tr>
<td>OBV/PTV/r + DSV + RBV</td>
<td>140/149</td>
<td>94%</td>
<td>96%</td>
</tr>
<tr>
<td>SOF/LDV + RBV</td>
<td>66/70</td>
<td>94%</td>
<td>97%</td>
</tr>
<tr>
<td>SOF/VEL³</td>
<td>49/51</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>SOF/VEL/VOX⁴</td>
<td>47/49</td>
<td>96%</td>
<td>96%</td>
</tr>
<tr>
<td>GLE/PIB⁵</td>
<td>151/157</td>
<td>96%</td>
<td>98%</td>
</tr>
</tbody>
</table>

SVR12 among former/recent PWID

<table>
<thead>
<tr>
<th>Study</th>
<th>SVR12 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norton 2017</td>
<td>96%</td>
</tr>
<tr>
<td>Hull 2016</td>
<td>89%</td>
</tr>
<tr>
<td>Conway 2016</td>
<td>95%</td>
</tr>
<tr>
<td>Bouscaillou 2017</td>
<td>88%</td>
</tr>
<tr>
<td>Powis 2017</td>
<td>87%</td>
</tr>
<tr>
<td>Read 2017</td>
<td>82%</td>
</tr>
<tr>
<td>Litwin 2017</td>
<td>95%</td>
</tr>
<tr>
<td>Sulkowski 2017</td>
<td>90%</td>
</tr>
<tr>
<td>Mazhnaya 2017</td>
<td>86%</td>
</tr>
</tbody>
</table>

Lost to follow-up post-treatment in the “real-world”

<table>
<thead>
<tr>
<th>SVR12 (%)</th>
<th>ITT</th>
<th>mITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>87%</td>
<td>60</td>
<td>69</td>
</tr>
<tr>
<td>91%</td>
<td>60</td>
<td>66</td>
</tr>
<tr>
<td>82%</td>
<td>59</td>
<td>72</td>
</tr>
<tr>
<td>91%</td>
<td>59</td>
<td>65</td>
</tr>
</tbody>
</table>

Recent PWID – The SIMPLIFY Study (SOF/VEL)

- 100% injecting in past 6 months, 35% G1a, 58% G1, 9% cirrhosis, DAA-treatment naïve
- No virological failures, no viral relapse, 1 case of reinfection

**ETR**
- 99/103
- 96%

**SVR12**
- 97/103
- 94%
We need to acknowledge and accept that HCV reinfection will occur.
What is the risk of HCV reinfection following therapy?

Not calculated among people with recent injecting post-therapy.
Specific issues on HCV reinfection for PWID

- **Acknowledgement**: there will be cases of HCV reinfection; if there are no cases, it is not a current PWID population

- **Harm reduction optimisation (NSP, OST access)**: HCV reinfection incidence will reflect HCV incidence in the setting

- **Rapid scale-up**: a slow scale-up will create HCV “susceptible” PWID without reduction in viraemic pool

- **Individual-level strategies**: treatment of injecting partners crucial

- **Access to re-treatment**: without stigma and discrimination

- **Community engagement and partnership**: use of peer workers
Testing, diagnosis, and linkage to care will be a major barrier moving forward
HCV care cascade among PWID (IFN-era)

Advances in diagnostics and point-of-care testing

Rapid diagnostic tests

Dried blood spot testing

Point of care and random access
HCV RNA testing
Finger-stick testing for HCV RNA detection

- Relatively easy-to-use point-of-care HCV RNA test – GeneXpert in many LMIC
- Real-world performance for HCV RNA quantification very good
  - Venepuncture HCV Viral Load – Sensitivity – 99%, Sensitivity 96%\(^1\)
  - Modified finger-stick assay – Sensitivity – 98%, Sensitivity 99%\(^2\)
  - Xpert® HCV Viral Load Fingerstick - Sensitivity – 100%, Sensitivity 100%\(^3\)
- One step closer to a single-visit diagnosis (needs to be more “rapid”)
Moving to a single-visit hepatitis C diagnosis

Visit #1
- Anti-HCV antibody (Physician)

Visit #2
- Phlebotomy (Phlebotomist)
- Central Lab
- Antibody test 1-2 weeks

Visit #3
- Receive diagnosis (Physician)

Visit #4
- Phlebotomy (Phlebotomist)
- Central Lab
- RNA test 1-2 weeks

Visit #5
- Receive diagnosis (Physician)

Dried blood spot sample (Health care worker)
- Antibody test 1-2 weeks

Rapid anti-HCV antibody test and HCV RNA and diagnosis (Health care worker)

Increased time, visits and lost of follow up

Grebely J Exp Rev Mol Diag 2017
Simplification of models of care and interventions will be crucial to achieve HCV elimination among PWID
What is a model of care?
Settings, services, and providers

**Settings**
- Sexual health
- Drug and alcohol clinics
- Community health centres
- Primary health care / GPs
- Prisons

**Services**
- NSP services

**Providers**
- Task-shifting
  - Specialists
  - Drug and alcohol specialist
  - Primary care providers
  - Nurses
  - Peer support workers
  - Others
Need to move towards simplified models of HCV care

- Many programs for HCV treatment are built upon interferon-era

- Need to move towards simplification of existing models

- Not at the expense of strengthening foundation for drug user health

Modified from John Dillon
Remaining challenges for HCV elimination in PWID
The burden of HCV among PWID is considerable

- 8.2M (4.7-12.4) PWID are HCV antibody positive (52%)
- 4 countries account for 51% of burden (Russia, United States, China, and Brazil)
Harm reduction services remain inadequate

Reimbursement restrictions must be removed

- 46% >F2 (advanced disease)
- 17% drug/alcohol use
- 94% specialist prescribing

Key features of Australian DAA access

- Several DAA regimens subsidised since March 2016
- No restrictions based on liver disease stage or drug and alcohol use
- No cap on number of patients treated per year
- Risk-sharing arrangement with pharma, with capped annual expenditure
- Broad practitioner base: gastro/hepatology, ID, other specialists, and GPs; Public hospital (S100) and community pharmacy (S85) dispensed
- Retreatment (including for reinfections) allowed
- Co-payment: $AUS 7-38/month
HCV treatment in Australia: 1997-2017

HCV treatment in Australia: 1997-2017

IFN-free DAA = 61,085
(26% chronic HCV)

* extrapolated

Australia – Treatment among PWID

Annual Needle Syringe Program Survey (n=2,500):

HCV treatment among chronic HCV (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>20</td>
</tr>
</tbody>
</table>

HCV RNA+ (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>47</td>
<td>28</td>
</tr>
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</table>
HCV treatment in Australia: Prescriber type

Kirby Institute 2017 (http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)
Task shifting to community-based non-specialist providers

- Three hour education and training
- Overall SVR12 following sofosbuvir/ledipasvir was 87%
- No difference by provider type: NPs, 90%; PCPs, 88%; and specialists, 85%

<table>
<thead>
<tr>
<th>Provider</th>
<th>SVR Rate</th>
<th>Patients With SVR/Total Patients, n/N</th>
<th>SVR Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NP 1</td>
<td>0.77</td>
<td>33/43</td>
<td></td>
</tr>
<tr>
<td>NP 2</td>
<td>1.00</td>
<td>12/12</td>
<td></td>
</tr>
<tr>
<td>NP 3</td>
<td>0.80</td>
<td>4/5</td>
<td></td>
</tr>
<tr>
<td>NP 4</td>
<td>1.00</td>
<td>30/30</td>
<td></td>
</tr>
<tr>
<td>NP 5</td>
<td>0.92</td>
<td>55/60</td>
<td></td>
</tr>
<tr>
<td>PCPs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCP 1</td>
<td>0.75</td>
<td>24/32</td>
<td></td>
</tr>
<tr>
<td>PCP 2</td>
<td>1.00</td>
<td>19/19</td>
<td></td>
</tr>
<tr>
<td>PCP 3</td>
<td>0.88</td>
<td>43/49</td>
<td></td>
</tr>
<tr>
<td>PCP 4</td>
<td>0.88</td>
<td>21/24</td>
<td></td>
</tr>
<tr>
<td>PCP 5</td>
<td>0.89</td>
<td>32/36</td>
<td></td>
</tr>
<tr>
<td>Specialists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist 1</td>
<td>0.77</td>
<td>47/61</td>
<td></td>
</tr>
<tr>
<td>Specialist 2</td>
<td>0.85</td>
<td>50/59</td>
<td></td>
</tr>
<tr>
<td>Specialist 3</td>
<td>0.89</td>
<td>34/38</td>
<td></td>
</tr>
<tr>
<td>Specialist 4</td>
<td>0.76</td>
<td>13/17</td>
<td></td>
</tr>
<tr>
<td>Specialist 5</td>
<td>0.94</td>
<td>35/37</td>
<td></td>
</tr>
<tr>
<td>Specialist 6</td>
<td>0.82</td>
<td>64/78</td>
<td></td>
</tr>
</tbody>
</table>

Key populations for HCV elimination efforts

- Former PWID
  - N=180,000 with chronic HCV

- Current PWID
  - N=38,000 with chronic HCV
  - PWID in OST
    - N=24,000 with chronic HCV

- Prisoners
  - N=40,000
  - Chronic HCV 25%
    - N=10,000
Remaining challenges for HCV elimination among PWID

- Further work is needed to address drug user health for PWID
- Continue to address stigma, discrimination, and HCV awareness
- Further simplification of testing and treatment
- One size will not fit all – different settings will require different interventions
- Continue to engage people in care other than HCV
Remaining challenges for HCV elimination among PWID

• Need to remove disease-stage reimbursement restrictions (double restriction)
• Task shifting to community-based non-specialist providers
• Education and training of providers and front-line workers
• Reinfection needs to be acknowledged and accepted
• Low and middle-income country setting (cost of testing, treatment, barriers)
• Act regionally, but think globally (micro-elimination)
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