Diagnosis and treatment of acute HCV in an interferon free era: Does it really matter?

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What is ‘acute HCV’?
Diagnosing acute HCV

Traditionally defined as the *first 6 months* after infection

1. Documented HCV antibody seroconversion
2. Clinical illness with jaundice (15-20%)
3. New rise in ALT without alternate cause and positive HCV RNA
4. Low $<10^4$ or fluctuating $>1$ log HCV RNA
NEAT consensus paper 2011

• Preferred criteria (Grade A, Level II)
  (1) Positive antibody in the presence or absence of a positive HCV RNA and a documented negative antibody or HCV RNA in the previous 12 months

• Alternative criteria (Grade B, Level III)
  Positive HCV RNA with: (1) A) an acute rise in ALT > 10x ULN or an acute rise in ALT >5X ULN, with documented normal ALT within 12m and (2) and exclusion of other causes of acute hepatitis.

*Potential duration of infection up to 1 year*
Recent HCV infection as defined by:

- an initial positive anti-HCV antibody within 6 months of enrolment and either:
  
  (i) a negative anti-HCV antibody in the 2 years prior to the initial positive anti-HCV antibody; or
  
  (ii) acute clinical hepatitis C (jaundice or ALT level > 10x ULN) within 12 months of the initial positive anti-HCV antibody

Maximal estimated duration of infection 18 months
Potential duration of infection up to 2.5 years
ACUTE

RECENTLY ACQUIRED

(replace with the correct term)
Australia: estimated incidence of HCV

Currently approximately 5-6,000 new HCV infections pa

Razali et al 2007,
KI Annual Surveillance Report
Diagnoses of recent HCV by exposure category

Table 2.1.13  Number of diagnoses of newly acquired hepatitis C infection, 2008 - 2012, by exposure category, year and sex

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>T</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Injecting drug use</td>
<td>160</td>
<td>95</td>
<td>255</td>
<td>164</td>
<td>95</td>
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<tr>
<td>Sexual contact</td>
<td>6</td>
<td>8</td>
<td>14</td>
<td>7</td>
<td>8</td>
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<tr>
<td>Blood/tissue recipient</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Skin penetration procedure</td>
<td>6</td>
<td>4</td>
<td>10</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Healthcare exposure</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>11</td>
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<tr>
<td>Household contact</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
<td>9</td>
<td>23</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>Undetermined</td>
<td>30</td>
<td>27</td>
<td>57</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>219</td>
<td>146</td>
<td>365</td>
<td>241</td>
<td>155</td>
</tr>
</tbody>
</table>

1  Totals include diagnoses in people whose sex was not reported.

Source: National Notifiable Diseases Surveillance System
Newly acquired hepatitis C notifications, 2004 – 2013, by year and age group

Source: National Notifiable Diseases Surveillance System
Does diagnosis of recent HCV matter?

163 participants enrolled in ATAHC

HCV RNA positive at screening and eligible for treatment (n=146)

Initiated treatment for HCV (n=111)

17 participants HCV RNA negative at screening

High treatment uptake (79%)

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
<th>AOR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tertiary education or greater, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No</td>
<td>0.41</td>
<td>0.17-0.96</td>
<td>0.037</td>
<td>0.43</td>
<td>0.17-1.08</td>
<td>0.071</td>
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<tr>
<td>Full-time or part-time employment, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No</td>
<td>0.39</td>
<td>0.17-0.91</td>
<td>0.030</td>
<td>0.44</td>
<td>0.18-1.10</td>
<td>0.080</td>
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<tr>
<td>Current depression, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
<td>1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Yes</td>
<td>0.29</td>
<td>0.11-0.78</td>
<td>0.014</td>
<td>0.40</td>
<td>0.14-1.17</td>
<td>0.093</td>
</tr>
<tr>
<td>Estimated duration of infection (wks)</td>
<td>1.02</td>
<td>1.00-1.05</td>
<td>0.063</td>
<td>1.03</td>
<td>1.00-1.06</td>
<td>0.035</td>
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<tr>
<td>Log_{10} HCV RNA (IU/L)</td>
<td>1.90</td>
<td>1.34-2.68</td>
<td>&lt;0.001</td>
<td>1.92</td>
<td>1.36-2.73</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Does diagnosis of recent HCV matter?
• Is diagnosing recent HCV important? ✓

• Is treating recent HCV important?
Treatment for recent HCV traditionally shortened

ATAHC: 24 weeks PEG (+RBV for HIV positive)

Treatment for recent HCV traditionally shortened

ATAHC II: Response guided PEG + RBV

- 56% allocated to shortened treatment duration

SVR 12 ITT

Overall: 71%
8 weeks: 85%
16 weeks: 100%
24 weeks: 73%
48 weeks: 100%

Martinello et al, manuscript in prep
ISG pattern is different in AHC versus CHC

Dill et al, Gastroenterology 2012
Can treatment for recent HCV be shortened in the era of IFN-free DAA therapy?

NO DATA YET!
## Registered clinical trials for DAAs in recent HCV infection

<table>
<thead>
<tr>
<th>Principal investigator and/or study group</th>
<th>Country, year commenced</th>
<th>Title</th>
<th>Duration of infection (months)</th>
<th>Study population</th>
<th>Estimated enrolment (n)</th>
<th>Regimen</th>
<th>Treatment duration (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matthews G</td>
<td>Australia 2012</td>
<td>DARE-C I</td>
<td>6-18</td>
<td>HCV GT 1; HIV+ and PWID eligible</td>
<td>15</td>
<td>PEG-IFN, RBV, TVR</td>
<td>8, 12 or 24</td>
</tr>
<tr>
<td>Rijnders B</td>
<td>Netherlands 2013</td>
<td>DAHHS</td>
<td>≤6</td>
<td>HCV GT 1 and HIV+; PWID eligible</td>
<td>60</td>
<td>PEG-IFN, RBV, BOC</td>
<td>12</td>
</tr>
<tr>
<td>Nelson M</td>
<td>UK 2014</td>
<td>CHAT</td>
<td>≤6</td>
<td>HCV GT 1 and HIV+; PWID eligible</td>
<td>20 (per arm)</td>
<td>PEG-IFN, RBV +/- TVR (1:1)</td>
<td>Response guided</td>
</tr>
<tr>
<td>Matthews G</td>
<td>Australia, New Zealand 2014</td>
<td>DARE-C II</td>
<td>≤12</td>
<td>GT 1-6; HIV+ and PWID eligible</td>
<td>20</td>
<td></td>
<td></td>
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<tr>
<td>Naggie S; AIDS Clinical Trials Group</td>
<td>US 2014</td>
<td>SWIFT-C</td>
<td>≤6</td>
<td>HCV GT 1-6 and HIV+; PWID eligible</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manns MP; HepNet</td>
<td>Germany 2014</td>
<td>HepNet Acute HCV IV</td>
<td>≤4</td>
<td>HCV GT 1; HIV+ and PWID ineligible</td>
<td>20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results to be presented at AASLD 2015
Current standard duration DAA therapy in naive patients

SVR12 %

- Naïve (12 wks)
- Naïve (8 wks)

- SOF/LED
- PTV/ODV/DSV/REB
- GZR/EBR
- SOF/DCV*
- SOF/GS-5816**

Zeuzem, NEJM2014; Afdhal, NEJM2014; Kowdley, NEJM2014; Feld, NEJM2014; Poordad, AASLD2014; Zeuzum, ILC2015; Kwo, ILC2015; Sulkowski, NEJM2014; Everson, ILC2014
Can therapy go shorter?

Triple NA/NS5A/PI: treatment naive, F0-3

REACT

A Randomised Controlled trial of IFN-free therapy for Hepatitis C during Recent infection

250 patients, 8 countries
Standard vs short duration or rolling very short duration cohorts
Adherence, risk behaviour, reinfection
• Is diagnosing recent HCV important?  ✔

• Is treating recent HCV important?  ✔
Why recent infection is still important?
Why recent infection is still important?
Why recent infection is still important?
The future: test and treat

- Annual screening high risk populations
- Rapid POC tests
- Very short course therapy ?4 weeks
- Simple single TOC