Recent data in
treatment of acute hepatitis C

Christoph Boesecke
Department of Medicine I
Bonn University Hospital
Bonn, Germany
Conflict of Interest

- Honoraria for lectures and/or consultancies from abbVie, BMS, Gilead, Janssen, MSD, Roche, ViiV.
- Research grants from Dt. Leberstiftung, DZIF, NEAT ID.
The advent of direct-acting antivirals- DAAs

Has revolutionized hepatitis C treatment.
not quite
Algorithm for Management of Acute HCV in Persons with Chronic HCV/HIV Co-infection

- **Initial presentation Acute HCV**
  - Week 4: Decay HCV-RNA
    - $< 2^{\text{log}_{10}}$
      - Treatment with PEG-IFN + RBV
      - Week 4: HCV-RNA level
        - Negative: Stop treatment after 24 weeks
        - Positive: Treatment for 48 weeks, stop treatment if $< 2^{\text{log}_{10}}$ decrease in HCV-RNA level at week 12
  - $\geq 2^{\text{log}_{10}}$
    - Week 12: HCV-RNA level
      - Negative: Serial HCV-RNA measurements throughout week 48 to confirm resolution
Treatment of acute HCV

10. In the absence of randomised, controlled data on the use of DAAs in the setting of acute HCV co-infection treatment with PEG-IFN and RBV should be based on an individual decision, weighing the known toxicities and longer treatment duration under dual therapy against a potentially strong patient wish from the co-infected person for early HCV cure, particularly in HIV-positive MSM with a higher risk of HCV transmission and in countries where DAAs will only be reimbursed in chronic HCV with ≥F3 fibrosis. After diagnosis of acute HCV, HCV-RNA should be measured 4 weeks later. Treatment can be discussed in persons without a decrease of 2^log_{10} of HCV-RNA at 4 weeks compared with initial HCV-RNA and in persons with persistent serum HCV-RNA 12 weeks after diagnosis of acute HCV, see Algorithm for Management of Acute HCV in Persons with HCV/HIV Co-infection. Early discontinuation of dual therapy is justified in persons experiencing significant side effects of PEG-IFN and/or RBV. Enrollment of persons with acute HCV co-infection in ongoing trials using IFN-free DAA combination therapy is strongly encouraged.
Treatment strategies beyond pegIFN + RBV

- pegIFN / RBV + HCV PI
  - Boceprevir
  - Telaprevir
- 1 DAA + RBV
  - Sofosbuvir + RBV
- 2 DAAs
  - Sofosbuvir + Simeprevir
  - Sofosbuvir + Ledipasvir
Dutch Acute Hepatitis C in HIV Study (DAHHS): SVR12 after 12w Boceprevir+ P/R

Gender: Male 100%
Race: Caucasian 93% non-Caucasian 7%
Genotype: 1a 95% b 5%
IL28B rs1297: CC 42.5% CT 50% TT 7.5%
Age: median 40 years (IQR 34-47)
CD4 count: median 0.56 E9/l (IQR 0.45-0.79)
Interval infection-treatment: median 22 weeks (IQR 16.5-25)
Baseline HCV Load: median 200.000 IU/ml (IQR 8.375-3.230.000)

Virological response in ITT patients:
- Wk 4: 40/55
- Wk 12 (EOT): 41/45
- Wk 24 (SVR12): 26/34

76.5%

Hullegie et al, CROI 2015 #669
Telaprevir in AHC

-12 -4 0 4 12 16 24 36

TVR + pIFN+RBV  Follow-up

Weeks

change ARVs

ETR  SVR 4  SVR 12  SVR 24

Total 16/19 16/19 16/19 16/19

Success rate 84% 84% 84% 84%

-> 89% (32/36) @AASLD 2015

63% (30/48) in comparator group:
Treated before licensing of or not suitable for telaprevir

Fierer et al, CID 2014 & AASLD 2015 #1112
• SVR24 was seen in 3/5 (60%) patients receiving PR alone and in 5/9 (56%) patients receiving TPV + PR.

• Of the 4 patients without SVR receiving TPV one experienced a viral breakthrough and 2 were non-responders; in one case HCV protease inhibitor associated mutations were selected under TPV (V36M, R155K).

Boesecke et al, under preparation
1074 Sofosbuvir and Ledipasvir versus Sofosbuvir and Simeprevir combination therapy in the management of acute hepatitis C: A randomized open label prospective clinical pilot study. SLAM C study. Interim data
Patrick Basu1,2, Niraj J. Shah3, Nimy John2, M. Aloysius2, Robert Brown4; 1Columbia University School of Physicians and Surgeons, Forest hills, NY; 2King’s County Hospital Medical Center, NY, New York, NY; 3James J. Peters VA Medical Center, Icahn School of Medicine at Mount Sinai, NY, New York, NY; 4Weill Cornell Medical College, New York, NY

1083 Sofosbuvir and Ribavirin for Six Weeks Is Not Effective Among People with Acute and Recently Acquired HCV Infection: The DARE-C II Study
Marianne Martinello1, Edward J. Gane2, Margaret Hellard3, Joe Sasadeusz4, David Shaw5, Kathy Petoumenos1, Tanya L. Applegate1, Jason Grebely1, Laurence Maire1, Philippa Marks1, David Cooper1, Gregory Dore1, Gail Matthews1 
1UNSW Australia, 2Auckland Hospital, 3Burnet Institute, 4Royal Melbourne Hospital, 5Royal Adelaide Hospital

1090 Sofosbuvir in the Treatment of Acute HCV Infection in HIV-infected Men
Daniel S. Fierer1, Zachary Barbati1, Douglas Dieterich2, Andrew L. Foster1,3, Tristan Morey1,3, Samuel Turner1,3 
1Mount Sinai School of Medicine, 2Icahn School of Medicine at Mount Sinai, 3James Cook University

1094 Sofosbuvir Plus Ribavirin Without Interferon For Treatment of Acute Hepatitis C Virus Infection in HIV-1 infected Individuals (SWIFT-C)
Susanna Naggie1, Kristen M. Marks2, Michael Hughes3, Daniel S. Fierer4, Arthur Y. Kim5, Kimberly Hollabaugh3, Jennifer Kiser6, Jhoanna Roa3, Bill Symonds2, Diana M. Brainard8, John G. McHutchison8, Marion G. Peters9, Raymond T. Chung5 
1Duke University Medical Center, 2Weill Cornell, 3Harvard, 4Mount Sinai School of Medicine, 5Massachusetts General Hospital, 6University of Colorado, 7Roivant, 8Gilead Sciences, Inc, 9University of California, San Francisco
SWIFT-C (ACTG 5327): SOF + RBV for 12 wks in AHC coinfection

<table>
<thead>
<tr>
<th></th>
<th>SOF/RBV 12 weeks N=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (quartiles)</td>
<td>45 (41, 47)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>6 (35)</td>
</tr>
<tr>
<td>Hispanic or Latino, n (%)</td>
<td>11 (65)</td>
</tr>
<tr>
<td>IV Drug Use Ever, n (%)</td>
<td>4 (24)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>4 (24)</td>
</tr>
<tr>
<td>GT 1, n (%)</td>
<td>15 (88)</td>
</tr>
<tr>
<td>First HCV infection, n (%)</td>
<td>17 (100)</td>
</tr>
<tr>
<td>Mean HCV RNA, log(_{10}) IU/mL ± SD</td>
<td>5.63 ± 1.76</td>
</tr>
<tr>
<td>Median time (days) from first evidence of infection (quartiles)</td>
<td>140 (121, 151)</td>
</tr>
<tr>
<td>Median CD4, cells/μL (quartiles)</td>
<td>498 (387, 612)</td>
</tr>
<tr>
<td>HIV RNA &lt;50 copies/mL, n (%)</td>
<td>15 (88)</td>
</tr>
<tr>
<td>Median ALT, mg/dL (quartiles)</td>
<td>181 (165, 284)</td>
</tr>
<tr>
<td>Median AST, mg/dL (quartiles)</td>
<td>106 (69, 159)</td>
</tr>
<tr>
<td>Median Tbili, mg/dL (quartiles)</td>
<td>0.70 (0.60, 0.80)</td>
</tr>
</tbody>
</table>
SWIFT-C (ACTG 5327): SOF + RBV for 12 wks in AHC coinfection

**Results: Viral Suppression Rates**

- Week 1: 2/17 (12%)
- Week 2: 5/17 (29%)
- Week 4: 12/17 (71%)
- Week 8: 17/17 (100%)
- Week 12: 17/17 (100%)
- SVR12: 10/17 (59%)

- 90% CI: 78%
- 60% Peg-interferon/RBV historic reference rate: 36%

Naggie et al, AASLD 2015 #1094
DARE-C II: SOF + RBV for 6 wks in AHC mono- and coinfection

- Mean age 42 years, 89% male (n=17), 74% HIV positive
- 68% GT1a (n=13), 26% GT3a infection (n=5)
- Injecting drug use (n=10, 53%), sexual exposure with a partner of the same sex (n=8, 42%)
- Median HCV RNA at screening 5.7 log10 IU/mL (IQR 5.0-6.3)
NYC: SOF + RBV for 12 wks in AHC coinfection

- SVR12 rate of 92% (11/12)
- 7 Caucasian, 2 Hispanic, 2 Black, 1 Asian
- 7 had CC and 5 had CT IL28B polymorphisms
- 10 GT 1a, 2 GT 1b
- Median baseline HCV-VL was 4.47 log10 IU/mL, although two had very high VL of >7 log10 IU/mL.
- Initiation of HCV treatment occurred after a median duration of 22 weeks (IQR 15, 34)
SLAM C: SOF + LDV or SMP in AHC monoinfection

- Group A (n=14): SOF 400 mg + LDV 90 mg (once daily) for 4 weeks
- Group B (n=15): SOF 400 mg + SIM 150 mg (once daily) for 8 weeks
- All patients GT 1 infection (7/7 GT1a/1b in group A and 7/8 GT1a/GT1b in group B, respectively)
- Mean viral load was 1,200 k in the SOF + LDV group and 1,600 k in the SOF + SIM group

<table>
<thead>
<tr>
<th></th>
<th>Group A SOF + LDV N=14</th>
<th>Group SOF + SIM N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 7, n, %</strong></td>
<td>13/14, 92.9%</td>
<td>13/15, 86.67%</td>
</tr>
<tr>
<td><strong>4 Weeks, n %</strong></td>
<td>14/14, 100% (ETVR)</td>
<td>14/15, 93.3% (1 dropped started IV drug use)</td>
</tr>
<tr>
<td><strong>8 Weeks, n, %</strong></td>
<td>14/14, 100%</td>
<td>14/15, 93.3% (ETVR)</td>
</tr>
<tr>
<td><strong>16 Weeks, n, %</strong></td>
<td>14/14, 100%, SVR12</td>
<td>14/15, 93.3%</td>
</tr>
<tr>
<td><strong>20 Weeks, n, %</strong></td>
<td>(1 dropped, transferred to the prison)</td>
<td>13/13, 100%, SVR12 (one was lost to follow-up-homeless)</td>
</tr>
<tr>
<td><strong>Retention</strong></td>
<td>13/14, 92.9%</td>
<td>13/15, 86.67%</td>
</tr>
</tbody>
</table>
Interim SVRs

- pegIFN / RBV + Telaprevir or Boceprevir: 56-84%

- Sofosbuvir + RBV: 21-92%

- Sofosbuvir + Simeprevir: 93%

- Sofosbuvir + Ledipasvir: 100%
Wait and see?

<table>
<thead>
<tr>
<th>Median age [years] (IQR)</th>
<th>Transmission risk [%]</th>
<th>Median CD4-cells [µl] (IQR)</th>
<th>HIV-RNA &lt;50copies /ml [%]</th>
<th>cART [%]</th>
<th>Median HCV-RNA [LU/ml] (IQR)</th>
<th>HCV-RNA &gt;800,000 IU/ml [%]</th>
<th>HCV-Genotype [%]</th>
<th>Median maximum ALT [U/l] (IQR)</th>
<th>Clinical symptoms [%]</th>
<th>Median Fibrosis Score [kPa] (IQR)</th>
<th>Median Follow-up [weeks] (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=41)</td>
<td>43 (37-47)</td>
<td>97.6</td>
<td>2.4</td>
<td>401 (360-736)</td>
<td>85</td>
<td>1.989.500 (633.000-6.670.000)</td>
<td>72.5</td>
<td>78</td>
<td>22</td>
<td>401 (153-616)</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Years since AHC diagnosis (# of available measurements)</th>
<th>1 (n=20)</th>
<th>2 (n=23)</th>
<th>3 (n=17)</th>
<th>4 (n=14)</th>
<th>5 (n=10)</th>
<th>6 (n=3)</th>
<th>7 (n=4)</th>
<th>8 (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median liver stiffness [kPa] (IQR)</td>
<td>7.7 (6-10)</td>
<td>7.0 (6-10)</td>
<td>6.3 (5-8)</td>
<td>6.4 (5-8)</td>
<td>4.4 (4-5)</td>
<td>7.7 (6-20)</td>
<td>7 (5.1-10)</td>
<td>8 (5-49.6)</td>
</tr>
</tbody>
</table>
### Declining treatment uptake in AHC

<table>
<thead>
<tr>
<th>Median age [years] (IQR)</th>
<th>Transmission risk [%]</th>
<th>Median CD4-cells [μl] (IQR)</th>
<th>HIV-RNA &lt;200 copies/ml [%]</th>
<th>cART [%]</th>
<th>Median HCV-RNA [IU/ml] (IQR)</th>
<th>HCV-RNA &gt;800,000 IU/ml [%]</th>
<th>HCV-Genotype [%]</th>
<th>Median maximum ALT [U/l] (IQR)</th>
<th>Clinical symptoms* [%]</th>
<th>Median time from diagnosis to treatment [weeks] (IQR)</th>
<th>SVR rate [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>41 (38-46)</td>
<td>99.4</td>
<td>6</td>
<td>466 (340-702)</td>
<td>86</td>
<td>2,190,460 (701,550-6,880,000)</td>
<td>67</td>
<td>77.2</td>
<td>18.9</td>
<td>349 (160-644)</td>
<td>19</td>
<td>8 (7-11)</td>
</tr>
</tbody>
</table>

Table 1: Baseline characteristics

![Pie chart showing percentage of different AHC episodes]

![Table showing annual rates of treatment initiation for new AHC diagnoses from 2007 to 2014]

**Table 2: Annual rates of treatment initiation for new AHC diagnoses from 2007 to 2014**

Licensing of first HCV PIs in Europe

Boesecke et al, CROI 2015, Abstract 670
HCV Seroconversions in EuroSIDA

Multivariable OR:
Tested for HCVAb: 1.07 (1.06 – 1.08; p<0.0001) per calendar year
Testing HCVAb positive: 1.04 (0.99 – 1.09; p=0.10) per calendar year

Boesecke et al, Liver Int 2015
<table>
<thead>
<tr>
<th>Study name</th>
<th>Coordinator</th>
<th>DAAs</th>
<th>HCV genotype</th>
<th>Duration (weeks)</th>
<th>HIV status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAHHS</td>
<td>Erasmus MC</td>
<td>BOC + pegIFN + RBV</td>
<td>1</td>
<td>12</td>
<td>pos</td>
</tr>
<tr>
<td>CHAT</td>
<td>UKB</td>
<td>TPV + pegIFN + RBV</td>
<td>1</td>
<td>12</td>
<td>pos</td>
</tr>
<tr>
<td>DARE-C I</td>
<td>Kirby Institute</td>
<td>TPV + pegIFN + RBV</td>
<td>1</td>
<td>8–24</td>
<td>neg + pos</td>
</tr>
<tr>
<td>DARE-C II</td>
<td>Kirby Institute</td>
<td>SOF + RBV</td>
<td>all</td>
<td>6</td>
<td>neg + pos</td>
</tr>
<tr>
<td>SWIFT-C</td>
<td>ACTG</td>
<td>SOF + RBV</td>
<td>all</td>
<td>8 vs. 12</td>
<td>pos</td>
</tr>
<tr>
<td>SOL</td>
<td>UKB</td>
<td>SOF + LDV</td>
<td>1, 4</td>
<td>6</td>
<td>pos</td>
</tr>
<tr>
<td>Hep-Net acute HCV</td>
<td>MHH</td>
<td>SOF + LDV</td>
<td>1</td>
<td>6</td>
<td>neg</td>
</tr>
</tbody>
</table>

Boesecke, Rockstroh, J Viral Hepat 2015
What about GT 3?
pegIFN + RBV for GT 3?

Fig. 3  RVR and SVR rates for GT 2/3

Boesecke et al, Infection 2015
Conclusions

- DAAs in acute HCV are well tolerated
  - if IFN- and 1st generation HCV PI-free

- SVR rates promising but impaired by
  - Too short treatment duration
  - High baseline viral load
  - Duration of acute infection
  - Emergence of RAVs
back-up
The reinfection incidence differed regionally, with the highest being in Paris (21.8/100py), followed by Vienna (16.8/100py), Berlin (8.2/100py), Duesseldorf (8.1/100py), and London/Chelsea Westminster (7/100py). The lowest incidence rate was seen in Hamburg (5.04/100py).
PROBE-C study

Observational cohort

Diagnosis Acute HCV

No therapy

Date of infection

Therapy

Baseline Week 48 Week 96 Week 144

probec@ukb.uni-bonn.de