Acute Hepatitis C in a HIV-infected patient

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Université Paris Diderot: site Bichat
• A 30-year-old MSM living with HIV since 2013
• Treated with antiretroviral medications since HIV diagnosis (current treatment Eviplera)
  - last CD4 count 464/mm3
  - last HIV RNA undetectable
• Having unprotected homo- sexual intercourse with multiple sexual partners
• Past history of anal condyloma, secondary syphilis, and herpes simplex virus infection
• Hepatitis C virus serology negative,
April 2015; Regular HIV follow-up tests showed:
- Liver function:
  - serum glutamic oxaloacetic transaminase 61 UI/l,
  - serum glutamic pyruvic transaminase 127 UI/l,
  - bilirubin 9 mmol/l,
  - gamma-glutamyl transferase 25 UI/l,
  - alkaline phosphatases 63UI/l,
- HCV viral load was 68.106 IU/ml (7.84 log).
- Acute hepatitis C virus (HCV) (genotype 4a)
Hepatitis C Virus Infections in the Swiss HIV Cohort Study: A Rapidly Evolving Epidemic

Gilles Wandeler,1,2,⁎ Thomas Gsponer,2 Andrea Bregenzer,3 Huldrych F. Günthard,4 Olivier Clerc,5 Alexandra Calmy,6 Marcel Stöckle,7 Enos Bernasconi,8 Hansjakob Furrer,1 Andri Rauch1,⁎; and the Swiss HIV Cohort Study

1Department of Infectious Diseases, Bern University Hospital and University of Bern, 2Institute of Social and Preventive Medicine, University of Bern, 3Cantonal Hospital, St Gallen, 4Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, 5University Hospital Lausanne, 6University Hospital Geneva; 7University Hospital Basel, and 8Regional Hospital, Lugano, Switzerland

In 2011 incidence = 4.09 /100 PY
Odds of HCV infection in HIV + compared to HIV – individuals

<table>
<thead>
<tr>
<th>Category</th>
<th>Subtotal (I²; p)</th>
<th>Odds ratio (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subtotal (I²=46.3%; p=0.045)</td>
<td>1.59 (1.0–2.52)</td>
<td>13.91</td>
</tr>
<tr>
<td>PWID</td>
<td>Subtotal (I²=91.2%; p&lt;0.0001)</td>
<td>6.00 (4.16–8.66)</td>
<td>36.38</td>
</tr>
<tr>
<td>Sex work</td>
<td>Subtotal (I²=44.8%; p=0.143)</td>
<td>3.11 (1.43–6.78)</td>
<td>5.68</td>
</tr>
<tr>
<td>MSM</td>
<td>Subtotal (I²=62.8%; p=0.030)</td>
<td>7.52 (4.43–12.77)</td>
<td>8.78</td>
</tr>
<tr>
<td>Prison inmates</td>
<td>Subtotal (I²=97.7%; p&lt;0.0001)</td>
<td>17.35 (7.62–39.51)</td>
<td>11.47</td>
</tr>
<tr>
<td>High risk</td>
<td>Subtotal (I²=95.6%; p&lt;0.0001)</td>
<td>6.80 (4.0–11.53)</td>
<td>23.78</td>
</tr>
<tr>
<td></td>
<td>Overall (I²=95.7%; p&lt;0.0001)</td>
<td>5.81 (4.53–7.45)</td>
<td>100.00</td>
</tr>
</tbody>
</table>
Question

• Do you treat this patient and when?
• If yes how?
Algorithm for Management of Acute HCV in Persons with 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: $\geq 2^{\text{log}_{10}}$
            - **Week 12** HCV-RNA level
              - Negative: HCV-RNA measurements at weeks 24, 36 and 48 to confirm spontaneous clearance
              - Positive: Treatment for 48 weeks, stop treatment if $< 2^{\text{log}_{10}}$ decrease in HCV-RNA level at week 12
**Recommended Treatment for Patients with Acute HCV Infection**

- If the practitioner and patient have decided that a delay in treatment initiation is acceptable, monitoring for spontaneous clearance is recommended for a minimum of 6 months. When the decision is made to initiate treatment after 6 months, treating as described for chronic hepatitis C is recommended. (see *Initial Treatment of HCV Infection*)
  Rating: Class Ila, Level C

- If a decision has been made to initiate treatment during the acute infection period, monitoring HCV RNA for at least 12 weeks to 16 weeks before starting treatment is recommended to allow for spontaneous clearance.
  Rating: Class Ila, Level C

**Recommended Regimens for Patients with Acute HCV Infection.**

- Owing to high efficacy and safety, the same regimens that are recommended for chronic HCV infection are recommended for acute infection.
  Rating: Class Ila, Level C
Instances, where benefits of early treatment outweigh waiting for HCV clearance.

- prevention of HCV transmission (eg, surgeon, IVDU, and or HIV+ MSM with sexual transmission),
- mitigation of clinical consequences (eg, patient with cirrhosis who is acutely superinfected with HCV),
- reduction in likelihood of loss-to-follow-up in patients who may not be engaged in care in 3-to-6 months.
• Early treatment will no longer confer a therapeutic clearance advantage over treatment in chronic infection as was so important in the IFN era.

a watch- and-wait strategy?
• Spontaneous clearance of HCV is significantly less frequent in HIV coinfection individuals but still occurs with reports of up to 15%

Boesecke et al. Curr Opin HIV AIDS 2015
Estimating the Time to Diagnosis and the Chance of Spontaneous Clearance During Acute Hepatitis C in Human Immunodeficiency Virus-Infected Individuals
• The risk of loss to follow-up
• Sexual transmission of the HCV may be most likely to occur during the acute phase of the disease (+++)
Directly acting antivirals for hepatitis C virus arrive in HIV/hepatitis C virus co-infected patients: from ‘mind the gap’ to ‘where’s the gap?’

Kate Childs\textsuperscript{a}, Chris Taylor\textsuperscript{b}, Douglas Dieterich\textsuperscript{c} and Kosh Agarwal\textsuperscript{a}

• « In most cases those with acute HCV will have minimal liver disease so the rationale for treatment could be viewed as ‘treatment as prevention’ rather than treatment for the individual. »

AIDS 2016
The patient with acute HCV infection should be counseled to reduce behaviors that could result in transmission, such as sharing of injection equipment or high-risk sexual practices.
Directly acting antivirals for hepatitis C virus arrive in HIV/hepatitis C virus co-infected patients: from ‘mind the gap’ to ‘where’s the gap?’

Kate Childs\textsuperscript{a}, Chris Taylor\textsuperscript{b}, Douglas Dieterich\textsuperscript{c} and Kosh Agarwal\textsuperscript{a}

• « It is these reinfection rates, coupled with the current high cost of DAA therapy, which could potentially present a barrier to treatment as an effective HCV prevention strategy »

AIDS 2016
• Treatment of acute HCV may remain more cost-effective chronic HCV because of the possibility of shorter treatment durations.
Risk of late relapse or re-infection with Hepatitis C after Sustained Virological Response: meta-analysis of 66 studies in 11,071 patients

Five-year rate (95%CI) of recurrence post-SVR, by risk group

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Studies</th>
<th>N</th>
<th>Avg. FU (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>43</td>
<td>9,419</td>
<td>4.1±2.1</td>
</tr>
<tr>
<td>(IDUs/prisoners)</td>
<td>16</td>
<td>819</td>
<td>2.9±1.6</td>
</tr>
<tr>
<td>HIV/HCV co-infected</td>
<td>7</td>
<td>833</td>
<td>3.1±1.2</td>
</tr>
</tbody>
</table>

Hill A et al, Abstract 654, CROI Seattle 2015
HCV reinfection incidence among individuals treated for recent infection

M. Martinello1 | J. Grebely1 | K. Petoumenos1 | E. Gane2 | M. Hellard3,4,5 | D. Shaw6 | J. Sasadeusz7 | T. L. Applegate1 | G. J. Dore1,8 | G. V. Matthews1,8

1Viral Hepatitis Clinical Research Program, Kirby Institute, UNSW Australia, Sydney, NSW, Australia

### TABLE 3  Incidence of HCV reinfection among participants treated for recent HCV infection

<table>
<thead>
<tr>
<th>Participant type</th>
<th>Cases of reinfection (n)</th>
<th>Participants at risk (n)</th>
<th>Person-years follow-up</th>
<th>Incidence/100 person-years</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed/possible reinfection</td>
<td>10</td>
<td>120</td>
<td>135</td>
<td>7.4</td>
<td>4.0, 13.8</td>
</tr>
<tr>
<td>Confirmed reinfection</td>
<td>8</td>
<td>120</td>
<td>135</td>
<td>5.9</td>
<td>3.0, 11.9</td>
</tr>
<tr>
<td>Confirmed persistent reinfection</td>
<td>5</td>
<td>120</td>
<td>135</td>
<td>3.7</td>
<td>1.5, 8.9</td>
</tr>
<tr>
<td>HCV mono-infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed/possible reinfection</td>
<td>3</td>
<td>56</td>
<td>67</td>
<td>4.5</td>
<td>1.4, 13.9</td>
</tr>
<tr>
<td>Confirmed reinfection</td>
<td>2</td>
<td>56</td>
<td>67</td>
<td>3.0</td>
<td>0.7, 11.9</td>
</tr>
<tr>
<td>Confirmed persistent reinfection</td>
<td>1</td>
<td>56</td>
<td>67</td>
<td>1.5</td>
<td>0.2, 10.6</td>
</tr>
<tr>
<td>HIV/HCV co-infectiona</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed/possible reinfection</td>
<td>7</td>
<td>64</td>
<td>68</td>
<td>10.3</td>
<td>4.9, 21.7</td>
</tr>
<tr>
<td>Confirmed reinfection</td>
<td>6</td>
<td>64</td>
<td>68</td>
<td>8.9</td>
<td>4.0, 19.7</td>
</tr>
<tr>
<td>Confirmed persistent reinfection</td>
<td>4</td>
<td>64</td>
<td>68</td>
<td>5.9</td>
<td>2.2, 15.7</td>
</tr>
</tbody>
</table>
Hepatitis C Treatment as Prevention of Viral Transmission and Liver-Related Morbidity in Persons Who Inject Drugs

Anthony Cousien,1,2 Viet Chi Tran,3 Sylvie Deuffic-Burban,1,2,4 Marie Jauffret-Roustide,5,6 Jean-Stéphane Dherin,7 and Yazdan Yazdanpanah1,2,8

Hepatology 2015
Question

• Do you treat this patient and when?
• If yes how?
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

• 29 patients with a diagnosis of acute hepatitis C
  - Group A (n=14): SOF 400 mg + LDV 90 mg (daily once) - 4 weeks
  - Group B (n=15): SOF 400 mg + SIM 150 mg (daily once) - 8 weeks

P. Basu, et al. AASLD 2015
<table>
<thead>
<tr>
<th>Undetectable</th>
<th>Group A SOF + LDV N=14</th>
<th>Group B SOF + SIM N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 weeks,</td>
<td>14/14, 100% (ETVR)</td>
<td></td>
</tr>
<tr>
<td>8 weeks,</td>
<td></td>
<td>14/15, 93.3% (ETVR)</td>
</tr>
<tr>
<td>16 weeks</td>
<td>14/14, 100%</td>
<td>14/15, 93.3%</td>
</tr>
<tr>
<td>20 weeks</td>
<td>13/13 (1 dropped, transferred to the prison)</td>
<td>13/15, (one was lost to follow-up- homeless)</td>
</tr>
</tbody>
</table>

High SVR with short-course DAA’s in acute hepatitis C with SVR (at 20 weeks) >90% in both groups. The drugs were well tolerated

P. Basu, et al. AASLD 2015
Sofosbuvir Plus Ribavirin Without Interferon
For Treatment of Acute Hepatitis C Virus
Infection in HIV-1 infected Individuals
(SWIFT-C)

• Single arm trial of the AIDS Clinical Trials Group (ACTG) (n=17)
• Safety and efficacy of 12 weeks of sofosbuvir (400mg/day) and weight based ribavirin (1000mg <75kg or 1200mg ≥75kg daily)
• Suppression of HCV in all participating HIV-infected men
• **High relapse rate (or re-infection) : 41%**
• Eight (47%) participants had a Grade 2 or higher adverse event (AE), but no serious AEs were reported

S. Naggie, et al. AASLD 2015
Ledipasvir/Sofosbuvir for 6 Weeks in HIV-Infected Patients with Acute HCV Infection

Genotype 1 or 4
Germany & UK
25/26 onART
Mean CD4 = 675

Rockstroh et al. CROI 2016
4 Virologic failures*  
22/26 SVR4

4 Virologic failures*  
20/26 SVR12

*3 patients relapsed, 1 was reinfected (GT 1a at baseline, 4d in post-treatment).

From bootstrapped 95% confidence intervals.

Rockstroh et al. CROI 2016
Six Weeks of Sofosbuvir/Ledipasvir (SOF/LDV) Are Sufficient to Treat Acute Hepatitis C Virus Genotype 1 Monoinfection: The HepNet Acute HCV IV Study

- 20 patients enrolled at 10 treatment centers in Germany from November 2014 through October 2015.

Figure 1. Virologic response in a study evaluating sofosbuvir/ledipasvir in 20 patients with acute HCV genotype 1 monoinfection.

abstract LB08]. J Hepatol. 2016;64(suppl 2).
Six Weeks of Sofosbuvir/Ledipasvir (SOF/LDV) Are Sufficient to Treat Acute Hepatitis C Virus Genotype 1 Monoinfection: The HepNet Acute HCV IV Study

Figure 2. Baseline HCV RNA and early virologic response in a study evaluating sofosbuvir/ledipasvir in 20 patients with acute HCV genotype 1 monoinfection.

EASL abstract LB08]. J Hepatol. 2016;64(suppl 2).
• To assess the rate of sustained virological response (SVR) 12 weeks after 8-week oral treatment with **grazoprevir 100mg/elbasvir 50mg (MRK-combo)** in patients with **acute hepatitis C** genotype 1 or 4 and co-infected with HIV (SAHIV).

• Treatment of **acute HCV with grazoprevir (MK-5172), elbasvir (MK-8742)** is effective and can be shortened from 12 to 8 weeks for HCV genotype 1 and 4 infection without substantial loss in efficacy **Dutch Acute HCV in HIV Study (DAHHS-2)**.
HCV testing; How often?

• A different follow-up in MSM patients?
• A different follow-up in MSM patients at risk for STI and/or Hep C?
  - History of STI infection
  - Behavioural factors
    • Seroadaptive behaviour for HIV (reduced condom use)
    • Mucosally traumatic practices
    • Mucosally administered recreational drugs (metamphetamine)
History of Past syphilis: Risk X 2.11 (95%CI = 1.39–3.20)
HCV testing; How often?

• A different follow-up in MSM patients?
• A different follow-up in MSM patients at risk for STI and/or Hep C?
  - History of STI infection
  - Behavioural factors
    • Seroadaptive behaviour for HIV (reduced condom use)
    • Mucosally traumatic practices
    • Mucosally administered recreational drugs (metamphetamine)
Estimating the Time to Diagnosis and the Chance of Spontaneous Clearance During Acute Hepatitis C in Human Immunodeficiency Virus-Infected Individuals

Distributions of the times from infection to diagnosis. Routine visits of human immunodeficiency virus-positive patients are assumed to occur every 3 months in scenario A (a) and every 6 months in scenario B (b).