Acute Hepatitis C
Are we finding it? Are we treating it?

Dr Emma Page MBBS MRCP MD
Chelsea and Westminster Hospital NHS Trust London
Are we finding it?

• Need sensitive & specific diagnostic tools
• Need a standardised case definition
• Need to identify at risk populations
• Need to determine suitability for screening
• Need national reporting of cases
Are we finding it?

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- Need a standardised case definition
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So how are we doing in finding AHC?
Are we finding it?

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Are we finding it?
Diagnostic tools

• ‘gold standard’ conversion to HCV Ab positivity with a positive HCV RNA BUT
  – Longitudinal monitoring
  – Most unaware of previous status
  – HCV Ab positive within 6 weeks of exposure - ? Delayed in immunocompromise
Are we finding it?
Diagnostic tools

- ‘gold standard’ conversion to HCV Ab positivity with a positive HCV RNA BUT
  - Longitudinal monitoring
  - Most unaware of previous status
  - HCV Ab positive within 6 weeks of exposure - ? Delayed in immunocompromise

HCV Ab seroconversion:
  - 25% baseline, 63% 3 months, 87% 6 months, 95% 12 months
  - Raise in ALT more sensitive than HCV Ab
  - 93% rise in ALT at 3 months post infection

**Delayed anti-HCV antibody response in HIV-positive men acutely infected with HCV**

Emma C. Thomson, Eleni Nastouli, Janice Main, Peter Karayiannis, Joseph Eliaahoo, David Muir and Myra O. McClure

*AIDS* 2009, 23:89–93

![Graph showing time to seroconversion](image)
Are we finding it?
Diagnostic tools

- Other options:
  1. ALT – cheap, sensitive, not specific
Are we finding it?
Diagnostic tools

• Other options:
  1. ALT – cheap, sensitive, not specific
  2. Combine Ag-Ab assay
     • Shorten diagnostic window period
     • Combined HCV Ag-Ab assay (MONOLISA HCV Ultra assay) vs HCV Ab alone
     • 68% vs 20% with first positive HCV RNA
     • BUT: ALT rise occurred earlier
Are we finding it?
Diagnostic tools

- Other options:
  1. ALT – cheap, sensitive, not specific
  2. Combine Ag-Ab assay
  3. Anti-HCV IgG Avidity Index
     - Diagnostic levels only occur within 8 days of onset of symptoms

Anti-HCV IgG avidity index in acute hepatitis C

Nicola Coppola, Raffaella Pisapia, Cecilia Marrocco, Salvatore Martini, Luisa Maria Vatiero, Vincenzo Messina, Gilda Tonziello, Caterina Sagnelli, Pietro Filippini, Felice Piccinino, Evangelista Sagnelli

Department of Public Medicine, Section of Infectious Diseases, Second University of Naples, Italy
Division of Infectious Diseases, Azienda Ospedaliera Sant'Anna e San Sebastianiano, Caserta, Italy

Received 26 February 2007; received in revised form 22 June 2007; accepted 11 July 2007
Are we finding it?
Diagnostic tools

- Other options:
  1. ALT – cheap, sensitive, not specific
  2. Combine Ag-Ab assay
  3. Anti-HCV IgG Avidity Index
  4. Anti-HCV IgM titre
     - IgM commonly detected in chronic HCV, need serial titres for AHC
Are we finding it?
Diagnostic tools

- Other options:
  1. ALT – cheap, sensitive, not specific
  2. Combine Ag-Ab assay
  3. Anti-HCV IgG Avidity Index
  4. Anti-HCV IgM titre
  5. Combined Anti-HCV IgG Avidity Index and IgM titre
    - AHC successfully identified in > 90% of symptomatic individuals from a single serum sample
Are we finding it?
Diagnostic tools

• Other options:
  1. ALT – cheap, sensitive, not specific
  2. Combine Ag-Ab assay
  3. Anti-HCV IgG Avidity Index
  4. Anti-HCV IgM titre
  5. Combined Anti-HCV IgG Avidity Index and IgM titre
  6. HCV RNA
     • As early as one week post infection
     • Gold standard for ongoing infection
     • Does not differentiate between acute and chronic infection
     • Expensive
Are we finding it?

• Need sensitive & specific diagnostic tools
• **Need a standardised case definition**
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Are we finding it?
Case definition (1)

• Allows accurate / reproducible diagnosis
• No standardised case definition in HIV+ or HIV-:
  – No single laboratory assay
  – Asymptomatic
  – Difficult to distinguish between AHC & exacerbation CHC
Are we finding it?
Case definition (1)

- Allows accurate / reproducible diagnosis
- No standardised case definition in HIV+ or HIV-:
  - No single laboratory assay
  - Asymptomatic
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Are we finding it?

Case definition (2)

Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference

The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel

Consensus recommendation: case definition acute hepatitis C virus infection

Preferred criteria (grade A, level II)

1. Positive anti-HCV immunoglobulin G (IgG) in the presence or absence of a positive HCV-RNA and a documented negative anti-HCV IgG in the previous 12 months.

2. Positive HCV-RNA and a documented negative HCV-RNA and negative anti-HCV IgG in the previous 12 months.

Requires longitudinal monitoring
Are we finding it?
Case definition (2)

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(2) Positive HCV-RNA and a documented negative HCV-RNA and negative anti-HCV IgG in the previous 12 months.

Alternative criteria (Grade B, Level III)
If historical data is lacking and relevant test results within the past year unavailable, acute hepatitis C may be diagnosed if the following criteria are met:

(1) Positive HCV-RNA regardless of anti-HCV IgG with any of the following two conditions:
   (a) An acute rise in ALT greater than 10 times the ULN.
   (b) An acute rise in ALT greater than five times the ULN, with documented normal ALT within 12 months. In individuals with a previously high ALT, an acute rise to 3.5 times their previous ALT is acceptable [14].

(2) Antihepatitis A virus IgM negative and antihepatitis B core IgM antibody negative, and exclusion of other causes of acute hepatitis.

Requires longitudinal monitoring
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Are we finding it?
Identifying at risk populations

- Ongoing IDUs
- HIV+ MSM..... Epidemic well documented
Are we finding it?
Identifying at risk populations: HIV+ve MSM

INCREASING INCIDENCE OF ACUTE HEPATITIS C IN HIV POSITIVE MEN SECONDARY TO SEXUAL TRANSMISSION: A NEW EPIDEMIC?

Chelsea and Westminster Hospital, London, UK

Background: To evaluate changes in acute HCV seroconversion and risk factors for acquisition of HCV within a dedicated HIV/GUM clinic.

Methods: We identified acute seroconverters for HCV from our sexual health and HIV cohort between January 1997 and December 2002. Demographic, clinical and risk factor data were analysed.

Results: 28 patients were identified, 26 of whom were HIV positive. There was a statistically significant increase in the incidence of documented HCV seroconversion, test for trend p value < 0.001. The only identifiable risk factor was unprotected sexual intercourse in 20 individuals. 4 patients had a history of current intravenous drug use (IDU). 9 individuals were diagnosed with infectious syphilis in the year preceding HCV seroconversion including 3 who were diagnosed with HCV and syphilis concurrently. 18 patients had asymptomatic seroconversion and the sole reason for HCV testing was to investigate abnormal liver function tests (LFTs). There was a statistically significant increase in the number of patients testing positive for HCV in our clinical cohort but no increase in the total number of patients having HCV tests. This makes it unlikely that our observations are due to a lowered threshold for testing.

Conclusion: The high number of individuals reporting unsafe sex, low documented IDU and high rate of concomitant syphilis infection suggests that sexual transmission is fuelling a significant increase in HCV seroconversion.

The 2nd IAS Conference on HIV Pathogenesis and Treatment
Abstract no. 972
Are we finding it?
Identifying at risk populations: HIV+ve MSM
Are we finding it?
Identifying at risk populations: HIV+ve MSM

Canada\(^{23}\): ~30 cases
Prevalence of chronic HCV/HIV\(^{24}\)
19%: 11,200

USA\(^{1,2}\): 55 cases
Prevalence chronic HCV/HIV\(^{12-14}\)
15 – 30%: 180,000 – 360,000

Lebanon\(^{22}\): 1 case
Prevalence of chronic HCV/HIV\(^{25}\)
49%: 1,500

Europe: 1068 cases
Prevalence chronic HCV/HIV\(^{14,15}\)
25%: 185,500
- UK\(^{3,4}\) 552
- Germany\(^{5,18,27}\) 157
- France\(^{6,7}\) 126
- Netherlands\(^{8,17}\) 97
- Belgium\(^{20}\) 69
- Swiss\(^{9}\) 23
- Italy\(^{10}\) 21
- Denmark\(^{21}\) 13
- Spain\(^{26}\) ~8

Taiwan\(^{28}\): 28 cases
Prevalence of chronic HCV/HIV\(^{29}\)
55%: 8,800

Australia\(^{11}\): 47 cases
Prevalence chronic HCV/HIV\(^{16,19}\)
< 1%: 1,000

Drugs:
80% deny IVDU
Non-IVDU common

Multivariate analysis:
– Non significant

Sex:
3 x as many sexual partners
7 x more likely to use internet

Multivariate analysis:
– Group sex: R/I UPAI & fisting
  – Participation in 2: OR 9
  – Participation in ≥ 3: OR 23
Drugs:
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Non-IVDU common

Multivariate analysis:
- Non significant

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Multivariate analysis:
- Group sex: R/I UPAI & fisting
  - Participation in 2: OR 9
  - Participation in ≥ 3: OR 23
Are we finding it?
Identifying at risk populations: HIV-ve MSM?

- Ongoing IDUs
- HIV+ MSM..... Epidemic well documented
- What about HIV- MSM?

  - Lower prevalence
    - HIV-
    - HIV+
      - Netherlands\(^1\): 0.4% vs 17.8%
      - Australia\(^2\): 1.1% vs 9.4%

  - What about incident HCV infection?.......

Are we finding it?  
Identifying at risk populations: HIV-ve MSM?

Brighton\textsuperscript{1}  
2000-2006  
n = 948  
25 episodes AHC: 0.30/100 py  
\begin{itemize}  
\item HIV-: 0.15/100 py\textsuperscript{*}  
\item HIV+: 1.12/100 py  
\end{itemize}  
\textsuperscript{*} Some subsequently diagnosed with HIV

America\textsuperscript{2}: MACS  
1984-2011  
n = 5310  
115 episodes AHC: 0.21/100py  
\begin{itemize}  
\item HIV-: 0.05/100 py  
\item HIV+: 0.42/100 py  
\end{itemize}

\textsuperscript{1} Richardson D. JID 2008;197:1213-1214.  \textsuperscript{2} Witt M. CID [Epub ahead of print]
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Are we finding it?  
Suitability for screening

<table>
<thead>
<tr>
<th>For</th>
<th>Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important health problem</td>
<td>Epidemic ongoing?</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>Cost effective?</td>
</tr>
<tr>
<td>Natural history known</td>
<td></td>
</tr>
<tr>
<td>Identifiable ‘at risk’ population</td>
<td>What tests:</td>
</tr>
<tr>
<td>Effective treatment</td>
<td>1. LFTs: cheap but not specific</td>
</tr>
<tr>
<td></td>
<td>2. HCV Ab: delayed in HIV+</td>
</tr>
<tr>
<td></td>
<td>3. HCV RNA: expensive (pooling?)</td>
</tr>
</tbody>
</table>
Are we finding it?
Screening – current incidence

EuroSIDA
n = 4296 HIV+
Irrespective route acquisition

From Jan 2002
- Baseline HCV Ab -
- 2 HCV Ab results

AHC = 150 in 19,178 py
Incidence: 0.79/100 py

1. Rockstroh JK et al. 11th International Congress on Drug Therapy in HIV Infection.
Are we finding it?
Screening – current incidence

EuroSIDA\(^1\)
2/3rds MSM

BUT
IDU highest incidence:
4.2/100 py vs 0.09/100 py

MSM incidence highest 2010 at > 1.5/100 py

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1. Rockstroh JK et al. 11\(^{th}\) International Congress on Drug Therapy in HIV Infection.
Are we finding it?
Screening – current incidence

Hepatitis C Virus Infections in the Swiss HIV Cohort Study: A Rapidly Evolving Epidemic

Gilles Wandeler,1,2 a Thomas Gepner,2 Andrea Bregenzer,2 Huldrych F. Günthard,4 Olivier Clerc,3 Alexandra Calmy,9 Marcel Stöckle,9 Enos Bernasconi,9 Hansjakob Furrer,1 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, Lucano, Switzerland

1998-2011
Assessed incident HCV infections in 3 HIV transmission groups:

<table>
<thead>
<tr>
<th>Transmission Group</th>
<th>n</th>
<th>1998 (100py)</th>
<th>2011 (100py)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDU</td>
<td>123</td>
<td>13.9</td>
<td>2.2</td>
</tr>
<tr>
<td>MSM</td>
<td>3333</td>
<td>0.2</td>
<td>4.1</td>
</tr>
<tr>
<td>HET</td>
<td>3144</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

Figure 2. Hepatitis C virus infection incidence rates by transmission group (shaded: 95% credible intervals). Abbreviations: HET, heterosexual; IDU, injection drug user; MSM, men who have sex with men; py, person-year.
Are we finding it?
Screening – current incidence

Incident Hepatitis C Virus Infection among US HIV-Infected Men Enrolled in Clinical Trials

Lynn E. Taylor,1 Marisa Hohbahr,2 Kunling Wu,3 Ronald J. Bosch,3 David L. Wyles,4 John A. Davis,5 Kenneth H. Mayer,1 Kenneth E. Sherman,6 and Karen T. Tashima7

1Department of Medicine, Brown University, Providence, Rhode Island; 2Department of Medicine, Stanford University, Stanford, California, and 3Statistical & Data Analysis Center, Harvard School of Public Health, Boston, Massachusetts; 4Department of Medicine, University of California, San Diego, La Jolla, California; and 5Department of Medicine, Ohio State University, Columbus, Ohio, 6Department of Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio

CID 2011:52 (15 March) • HIV/AIDS

ACTG LLRT cohort
Retrospective
1996-2008
n = 1830 HIV+ve men
>7000 py follow up
36 (2%) AHC: 75% denied IDU
0.51/100 py
Are we finding it?
Screening – current incidence

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n = 1830 HIV+ve men
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36 (2%) AHC: 75% denied IDU
0.51/100 py

Prevalent and Incident Hepatitis C Virus Infection Among HIV-Infected Men Who Have Sex With Men Engaged in Primary Care in a Boston Community Health Center

Boston Community Health Centre
Retrospective
1997-2009
n = 379 HIV+ve MSM
1408 py follow up
23 (6%) AHC: 66% denied IUD
1.63/100 py
Are we finding it?
Screening – current re-infection incidence

Lambers et al AIDS 2011¹:
- ? Incidence rate of HCV re-infection
- n = 56 with ETR
- n = 5 relapsed
- Genotype or clade switch
- 11/51 re-infected

Incidence re-infection: 15.2/100 py

cumulative incidence of re-infection was 33% (95% CI 16-50) in 2 years

1. Lambers FA et al. AIDS 2011;25;F21-F27
Are we finding it?
Screening – current re-infection incidence

Martin et al Coinfection 2013:\(^1\):

- Re-infection:
  1) change in genotype
  2) Resurgent RNA post SVR or SC
- 2004 to 2012
- 145 HIV+ MSM, 394 py fu

Incidence re-infection: 8.1/100 py

- SC 13%
- TC 76%

Stratified according to primary AHC outcome

- SC: 4.3/100 py (n=5)
- TC: 9.6/100 py (n=27)

1. Martin T et al. HIV & Hepatitis Coinfection Workshop, Rome 2013
Are we finding it?
Screening - cost effective?

Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference

The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel

AIDS 2011, 25:399–409

Consensus recommendation screening for acute HCV infection (grade A, level II, *grade C, level II)

(1) All newly diagnosed HIV individuals should be screened for anti-HCV antibody [42].

(2) HIV-infected MSM at risk for contracting acute hepatitis C infection should be screened at 6-month interval with ALT and annually with anti-HCV antibody.
### Screening strategies:

1. Symptom based
2. LFT 3 monthly
3. LFT 6 monthly
4. LFT 12 monthly
5. **LFT 6 monthly & HCV Ab 12 monthly**
6. LFT 3 monthly & HCV Ab 3 monthly
7. LFT 6 monthly & HCV RNA 6 monthly
8. LFT 6 monthly & HCV RNA 12 monthly
9. LFT 3 monthly & HCV RNA 3 monthly
10. LFT 6 monthly & HCV RNA 6 monthly

### Analyses

- Monte Carlo simulation model
- \( n = 10,000,000 \)
- US guideline concordant care
- Baseline prevalence of HCV 9.8%
- Initial cohort incidence: 0.51/100 py
- US $100,000 (£60,000) per QALY gained
- UK NICE $50,000 (£30,000) per QALY gained

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Linas et al. CID 2012;55;279-290
Are we finding it? Screening - cost effective?

Mathematical model: HIV+ MSM; Linas et al

Analyses

NEAT & 3 monthly LFTs: larger gain in QALE at a lower cost/QALY gained

Rt of efficiency frontier:
1. lower QALE at higher cost
2. higher cost/QALY gained
Are we finding it?
Screening - cost effective?

Mathematical model: HIV+ MSM; Linas et al
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Are we treating it?
## Are we treating it?

<table>
<thead>
<tr>
<th>Author/country Study type</th>
<th>year</th>
<th>n</th>
<th>risk</th>
<th>SC</th>
<th>Rx groups</th>
<th>Time to Rx</th>
<th>Duration (weeks)</th>
<th>SVR</th>
<th>SVRG1/4</th>
<th>SVRG2/3</th>
<th>RVR PPV</th>
<th>RVR NPV</th>
<th>EVR NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gileece UK, R &amp; P</td>
<td>2005</td>
<td>50</td>
<td>MSM 88% IDU 2%</td>
<td>24%</td>
<td>piFN+RBVwb</td>
<td>4wks</td>
<td>24</td>
<td>59%</td>
<td>55%(12/20)</td>
<td>100%(4/4)</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
</tr>
<tr>
<td>Krusk Russia, P</td>
<td>2005</td>
<td>17</td>
<td>MSM 5% IDU 87%</td>
<td>n/a</td>
<td>n/a</td>
<td>24</td>
<td>53%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
</tr>
<tr>
<td>Vogel Germany, P</td>
<td>2006</td>
<td>47</td>
<td>MSM 81% IDU Unknown 19%</td>
<td>25%</td>
<td>Overall piFN (n=15) piFN+RBVwb (n=21)</td>
<td>7wks</td>
<td>59%(16/27)</td>
<td>71%(5/7)</td>
<td>n/m</td>
<td>n/m</td>
<td>91%(c)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schnuriger France, P</td>
<td>2009</td>
<td>38</td>
<td>MSM 100%</td>
<td>13%</td>
<td>piFN+RBV800</td>
<td>18wks</td>
<td>65%</td>
<td>63%(12/19)</td>
<td>100%(1/1)</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td></td>
</tr>
<tr>
<td>Matthews ATAHC, P</td>
<td>2009</td>
<td>27</td>
<td>MSM 56% IDU 44%</td>
<td>7%</td>
<td>piFN+RBVwb</td>
<td>30wks</td>
<td>74%</td>
<td>64%(7/11)</td>
<td>100%(9/9)</td>
<td>75%</td>
<td>13%</td>
<td>stopping rule</td>
<td></td>
</tr>
<tr>
<td>Fierer USA, R</td>
<td>2009</td>
<td>53</td>
<td>MSM 100%</td>
<td>9%</td>
<td>piFN+RBVwb</td>
<td>24-48wks</td>
<td>75%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
</tr>
<tr>
<td>Stellbrink Germany, R</td>
<td>2010</td>
<td>72</td>
<td>MSM 100%</td>
<td>19%</td>
<td>piFN+RBVwb</td>
<td>90 days</td>
<td>71%</td>
<td>63%(21/33)</td>
<td>100%(9/9)</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td></td>
</tr>
<tr>
<td>Piroth HEPAIG, R</td>
<td>2010</td>
<td>53</td>
<td>MSM 100%</td>
<td>15%</td>
<td>piFN+RBVwb</td>
<td>9/15</td>
<td>82%</td>
<td>60%(7/11)</td>
<td>100%(15/15)</td>
<td>n/a</td>
<td>n/a</td>
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<td></td>
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<tr>
<td>Thomson UK, R</td>
<td>2011</td>
<td>112</td>
<td>MSM 100%</td>
<td>15%</td>
<td>piFN+RBVwb</td>
<td>12wks</td>
<td>66%</td>
<td>n/m</td>
<td>n/m</td>
<td>87%</td>
<td>n/m</td>
<td>85%(c)</td>
<td></td>
</tr>
<tr>
<td>Obermeier Germany, R</td>
<td>2011</td>
<td>319</td>
<td>MSM 93% IDU 1%</td>
<td>26%</td>
<td>piFN+RBV +/- wb (135)</td>
<td>13wks</td>
<td>69%</td>
<td>n/m</td>
<td>n/m</td>
<td>83%</td>
<td>n/m</td>
<td>83%</td>
<td>n/m</td>
</tr>
<tr>
<td>Arends Netherlands, P</td>
<td>2011</td>
<td>23</td>
<td>no RVR add RBVwb (3)</td>
<td>4%</td>
<td>piFN+RBVwb</td>
<td>n/m</td>
<td>37%</td>
<td>n/a</td>
<td>71%</td>
<td>83%</td>
<td>stopping rule</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lambers Netherlands, P</td>
<td>2011</td>
<td>52</td>
<td>MSM 100%</td>
<td>4%</td>
<td>piFN+RBVwb</td>
<td>21wks</td>
<td>77%</td>
<td>95%</td>
<td>91%</td>
<td>91%</td>
<td>n/a</td>
<td>10%</td>
<td>10%</td>
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<td>Dorward UK, R</td>
<td>2011</td>
<td>34</td>
<td>MSM 100%</td>
<td>3%</td>
<td>piFN+RBVwb</td>
<td>14wks</td>
<td>91%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/a</td>
<td>n/a</td>
<td>stopping rule</td>
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<td>2012</td>
<td>38</td>
<td>MSM 95%</td>
<td>3%</td>
<td>piFN+RBVwb</td>
<td>12wks</td>
<td>47%</td>
<td>n/m</td>
<td>n/m</td>
<td>92%</td>
<td>80%</td>
<td>stopping rule</td>
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<tr>
<td>Webster UK</td>
<td>2013</td>
<td>74</td>
<td>MSM 100%</td>
<td>20%</td>
<td>piFN+RBVwb</td>
<td>24wks</td>
<td>83%</td>
<td>n/m</td>
<td>n/m</td>
<td>100%</td>
<td>71%</td>
<td>100%</td>
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</tr>
</tbody>
</table>
Are we treating it?

- is ribavirin needed?
- how long to treat?
- what about DAA?
Are we treating it?
What to treat with: Is ribavirin needed?

Recommendations

54. Patients with acute HCV infection should be considered for interferon-based anti-viral therapy (Class I, Level B).

55. Treatment can be delayed for 8 to 12 weeks after acute onset of hepatitis to allow for spontaneous resolution (Class IIa, Level B).

56. Although excellent results were achieved using standard interferon monotherapy, it is appropriate to consider the use of peginterferon because of its greater ease of administration (Class I, Level B).

57. Until more information becomes available, no definitive recommendation can be made about the optimal duration needed for treatment of acute hepatitis C; however, it is reasonable to treat for at least 12 weeks, and 24 weeks may be considered (Class IIa, Level B).

58. No recommendation can be made for or against the addition of ribavirin and the decision will therefore need to be considered on a case-by-case basis (Class IIa, Level C).

EASL Clinical Practice Guidelines: Management of hepatitis C virus infection

European Association for the Study of the Liver

Recommendations

1. Pegylated IFN-α monotherapy (pegylated IFN-α2a, 180 μg/week or pegylated IFN-α2b, 1.5 μg/kg/week, for 24 weeks) is recommended in patients with acute hepatitis C and obtains viral eradication in >90% of patients (B2).

2. Patients failing to respond should be re-treated according to the standard of care for chronic hepatitis C (C2).
Multiple small cohort studies:
- 4 included IFN monotherapy
  - 33 individuals
  - (different: durations, IFN, genotypes)
  - SVR 35%-80% / overall 57%
- Arends et al 20111
  - 19 patients treated (all G1/4)
  - If no RVR: RBV added (3/12)
  - Treated for 24-48 weeks
  - SVR: 37%
- 12 included PegIFN + RBV
  - 473 individuals
  - SVR 48%-84%
  - Overall 70%

---

### Table: HCV treatment outcomes

<table>
<thead>
<tr>
<th>Author/Country Study type</th>
<th>Year</th>
<th>n</th>
<th>SC</th>
<th>Risk</th>
<th>Rx groups</th>
<th>Time to Rx</th>
<th>Duration (weeks)</th>
<th>SVR</th>
<th>SVRG1/4</th>
<th>SVRG2/3</th>
<th>RVR</th>
<th>RVR FVV</th>
<th>RVR NPV</th>
<th>EVR NPV</th>
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<tbody>
<tr>
<td>Gilead UK, N &amp; P</td>
<td>2005</td>
<td>50</td>
<td>M</td>
<td>36%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>48</td>
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<td>n/m</td>
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<td>n/m</td>
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<td>70%</td>
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<td>n/m</td>
<td>n/m</td>
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<td>n/m</td>
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<tr>
<td>Schnollr Germany, P</td>
<td>2009</td>
<td>19</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
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<td>n/m</td>
<td>n/m</td>
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<td>80%</td>
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<tr>
<td>Forier USA, R</td>
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<td>15</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
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<td>48</td>
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<td>n/m</td>
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<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
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<td>100%</td>
<td>PegIFN + RBV</td>
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<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
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<tr>
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<td>PegIFN + RBV</td>
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<td>95%</td>
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<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
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</tr>
<tr>
<td>Arends Netherlands, P</td>
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<td>23</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
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<tr>
<td>Lammers Netherlands, P</td>
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<tr>
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<td>34</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
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<td>n/m</td>
<td>n/m</td>
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<td>n/m</td>
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<tr>
<td>Lagno Spain, R</td>
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<td>38</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
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<td>n/m</td>
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<tr>
<td>Webster UK, R</td>
<td>2013</td>
<td>74</td>
<td>M</td>
<td>100%</td>
<td>PegIFN + RBV</td>
<td>6+6</td>
<td>24</td>
<td>95%</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
<td>n/m</td>
</tr>
</tbody>
</table>

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HIV-/AHC PegIFN vs. HIV+/AHC PegIFN/RBV

24 wks treatment

80% adherent: n = 89 – analyzed

- PegIFN: SVR 63% vs. PegIFN/RBV: SVR 75%

- wk 12 HCV RNA decline greater in PegIFN/RBV
  - Duration AHC ≥ 26wks (75%)
  - Unfavourable IL28B genotype
Are we treating it?

• is ribavirin needed?
• **how long to treat?**
• what about DAA?
Are we treating it?
How long to treat: 24 weeks vs 48 weeks

• In AHC mono-infection 24 weeks
• Cohort studies in AHC co-infection duration varied: 24 wks vs 48 wks
• In chronic HCV viral kinetics predict duration
• In acute HCV can viral kinetics predict duration required?
Are we treating it?
How long to treat: 24 weeks vs 48 weeks

- In AHC mono-infection 24 weeks
- Cohort studies in AHC co-infection duration varied: 24wks vs 48wks
- In chronic HCV viral kinetics predict duration
- In acute HCV can viral kinetics predict duration required?
  - European multi-centered cohort study¹
    - If RVR+ SVR 93%
    - If 20wks treatment post 1\textsuperscript{st} negative HCV RNA SVR 96% vs 20% if < 20wks
    - ? 24wks sufficient if RVR+

Are we treating it?
How long to treat: 24weeks vs 48weeks

- In AHC mono-infection 24 weeks
- Cohort studies in AHC co-infection duration varied: 24wks vs 48wks
- In chronic HCV viral kinetics predict duration
- In acute HCV can viral kinetics predict duration required?
  - European multi-centered cohort study\(^1\)
    - If RVR+ SVR 93%
    - If 20wks treatment post 1\(^{st}\) negative HCV RNA SVR 96% vs 20% if < 20wks
    - ? 24wks sufficient if RVR+
  - Australian Trail in AHC (24 wks)\(^2\)
    - PPV RVR 75% - supports 24 wks in RVR+
    - NPV RVR 13% - ? 24wks sufficient if RVR-

Are we treating it?
How long to treat: 24 weeks vs 48 weeks

- In AHC mono-infection 24 weeks
- Cohort studies in AHC co-infection duration varied: 24wks vs 48wks
- In chronic HCV viral kinetics predict duration
- In acute HCV can viral kinetics predict duration required?
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    - If RVR+ SVR 93%
    - If 20wks treatment post 1\textsuperscript{st} negative HCV RNA SVR 96% vs 20% if < 20wks
    - ? 24wks sufficient if RVR+
  - Australian Trail in AHC (24 wks)²
    - PPV RVR 75% - supports 24 wks in RVR+
    - NPV RVR 13% - ? 24wks sufficient if RVR-
  - Laguno et al (24 wks)³
    - RVR+ SVR 92%
    - RVR- SVR 20%

Are we treating it?
How long to treat: 24 weeks vs 48 weeks

Treatment of acute hepatitis C virus infection in HIV-infected MSM: the effect of treatment duration

Femke A.E. Lambers, Kees Brinkman, Janke Schinkel, Ingrid J.B. Spijkerman, Richard Molenkamp, Roel A. Coutinho, Maria Prins, Jan T.M. van der Meer, on behalf of the MOSAIC (MSM Observational Study of Acute Infection with hepatitis C) study group

AIDS 2011, Vol 25 No 10

24 wks: n=50, SVR 71%
48 wks: n=50, SVR 79%

Those with no RVR
24 wks: SVR 40%
48 wks: SVR 64%
Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference

The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel

AIDS 2011, 25:399–409

Consensus recommendation on treatment of acute hepatitis C infection

(1) Pegylated IFN and weight-based ribavirin is recommended for the treatment of acute hepatitis C in HIV-infected patients (grade A, level II).

(2) Duration of treatment should be based on RVR [negative HCV-RNA at week 4 (evidence based on using a 61SU/ml cut-off to define negative HCV-RNA)], regardless of HCV genotype.

(a) In patients with RVR, treatment duration should be 24 weeks (AII).

(b) In patients without RVR, treatment duration of 48 weeks should be considered (BIII).

(c) In non-RVR patients not achieving a 2 log₁₀ drop in HCV-RNA at week 12, treatment can be discontinued (BIII).

Are we treating it?

How long to treat: 24 weeks vs 48 weeks

n=22 following NEAT guidelines:
RVR n=12: SVR 92%
No RVR n=10: SVR 90%
Are we treating it?

- is ribavirin needed?
- how long to treat?
- what about DAA?
Are we treating it?
Direct acting anti-virals for AHC

Are we treating it?
Direct acting anti-virals for AHC

-4 week  -0 week  4 week  12 week  24 week SVR 12

n = 40
Jul’11 to Sep’12

n = 13  non G1
n = 1  salvage ARVs with interactions
n = 5  uninsured
n = 5  seroconverted
n = 2  refused treatment

n = 20  treated

Are we treating it?
Direct acting anti-virals for AHC

DEMOGRAPHIGS
- Median age 44yrs
- 17 white, 2 hispanic, 1 black
- 18 G1a, 2 G1b
- IL28B: 4CT, 3TT, 13CC

Are we treating it?
Direct acting anti-virals for AHC

DEMOGRAPHIGS
• Median age 44yrs
• 17 white, 2 hispanic, 1 black
• 18 G1a, 2 G1b
• IL28B: 4CT, 3TT, 13CC

RESULTS
• ETR 85% (17/20)
• SVR4 85% (17/20)
• SVR12 82% (14/17)
• No relapse post ETR
• 3 failed: 2 VL at 4wk, 1 rebound 12wk

Acute hepatitis C
Are we finding it? Are we treating it?

Are we finding it?
• improved diagnostic tools
• standardised case definition
• screen at risk groups
• report cases

Are we treating it?
• When we find it – YES
• Use ribavirin
• Use RVR to determine duration
• DAA are the future