Dr Thomas Martin
Chelsea and Westminster Hospital, London
Hepatitis C virus reinfection among HIV positive men who have sex with men

TCS Martin
HIV/HCV Coinfection

- Liver disease is the leading non-AIDS cause of death in HIV infected individuals (14.5%)\(^1\)
- Hepatitis C virus (HCV) accounts for approximately two-thirds of liver disease in HIV infected individuals
- Coinfection with HIV leads to:
  - Reduced HCV spontaneous clearance rates of 20%
  - Increase in HCV related progression to cirrhosis by 2-3 fold\(^2\)
  - Reduction in HCV treatment success

HCV among HIV infected MSM

- Epidemic of sexually transmitted HCV occurring among the HIV infected men who have sex with men (MSM) population since early 2000s
- Transmission associated with high-risk sexual practices, ulcerating genital lesions and recreational drug use
- Reinfection with HCV following clearance has been documented although contribution to the epidemic is unknown

### Aim

1. Calculate HCV reinfection incidence among HIV infected MSM in London
2. Compare reinfection incidence between individuals who were either previously treated or spontaneously cleared their primary infection
3. Describe spontaneous clearance rates and sustained viral response (SVR) rates of HCV reinfection
Study Design

- Retrospective analysis of all HIV/HCV coinfectected individuals between 2004-2012 at Chelsea and Westminster Hospital

- Inclusion:
  - HIV infected MSM
  - No reported history of injecting drug use
  - Achieved HCV infection SVR through treatment or spontaneous clearance with at least one subsequent HCV PCR result
Definitions

Reinfection
- Any newly positive HCV RNA PCR 24 weeks or more following end of treatment or clearance of the virus; or
- Newly positive HCV RNA PCR within 24 weeks of end of treatment or clearance if reinfeeted with a different genotype

Following treatment

Following spontaneously clearance

Time to reinfection

Incident Infection | Treatment | 24 weeks | Reinfection

Incident Infection | Spontaneous Clearance | 24 weeks | Reinfection
## Study characteristics

<table>
<thead>
<tr>
<th>Incident infection</th>
<th>All incident infections</th>
<th>Primary infection</th>
<th>Treated HCV Infection</th>
<th>Spontaneously cleared HCV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Non-reinfected</td>
<td>Reinfection</td>
</tr>
<tr>
<td>Total</td>
<td>191</td>
<td>145</td>
<td>87</td>
<td>27</td>
</tr>
<tr>
<td>Median age (IQR)</td>
<td></td>
<td></td>
<td>41 (38-47)</td>
<td>41 (37-43)</td>
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<tr>
<td>Follow-up</td>
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<td>39 (34-43)</td>
<td>36 (35-42)</td>
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<tr>
<td>Median testing</td>
<td>112 (62-224)</td>
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<td>189 (89-343)</td>
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<tr>
<td>interval, days (IQR)</td>
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<td></td>
<td>99 (63-247)</td>
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<tr>
<td>cART use during</td>
<td>129 (89)</td>
<td>82 (94)</td>
<td>22 (81)</td>
<td>21 (81)</td>
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<tr>
<td>follow-up (%)</td>
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<td>4 (80)</td>
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<tr>
<td>Median peak ALT</td>
<td>38 (26-55)</td>
<td>254 (140-892)</td>
<td>58 (35-125)</td>
<td>226 (168-499)</td>
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<td>during follow up</td>
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<td>(IQR)</td>
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<tr>
<td>Median CD4 at last</td>
<td>547 (444-681)</td>
<td>429 (379-624)</td>
<td>531 (392-687)</td>
<td>397 (280-710)</td>
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<td>negative HCV RNA</td>
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<td>PCR/first positive</td>
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</table>

P < 0.0001
• Overall reinfection rate 7.8/100py (95% CI 5.8-10.5/100py)
• Post-treatment 8.0/100py vs. post-spontaneous clearance 4.2/100py (p=0.15)
• Second reinfection rate 23.2/100py
HCV reinfection outcomes

- Total of 54 reinfections
- 20% spontaneous clearance rate
- Treatment outcome with pegylated-interferon/Ribavirin
  - Genotype 1/4: 73% SVR (N=22)
  - Genotype 2/3: 100% SVR (N=2)
Limitations

- Retrospective study
- No phylogenetic analysis performed to confirm true reinfection
- Variable testing intervals with potential to affect results
Conclusion

• High rates of HCV reinfection among HIV infected MSM (7.8/100py)
  – Targeted sexual education for MSM who contract HCV infection
  – Enhanced surveillance of individuals who have previously been infected with HCV
  – Implications for cost efficacy of treatment
• Weak evidence for protective immunity following spontaneous clearance ($p=0.15$)
• Spontaneous clearance rate (20%) supports initial monitoring before treatment of reinfection
Thank you

- Co-authors: NK Martin\textsuperscript{2,3}, M Hickman\textsuperscript{2}, P Vickerman\textsuperscript{3}, EE Page\textsuperscript{1}, R Everett\textsuperscript{1}, BG Gazzard\textsuperscript{1}, M Nelson\textsuperscript{1}
  1. Chelsea and Westminster Hospital
  2. School of Social and Community Medicine, University of Bristol
  3. Department of Global Health and Development, London School of Hygiene and Tropical Medicine

- St Stephen’s AIDS Trust for financial support
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<td>Incident Genotype</td>
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<tr>
<td>1</td>
<td>97</td>
<td>67 (77)</td>
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<td>2</td>
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<td>1 (1)</td>
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<td>Median peak ALT</td>
<td>476 (251-1014)</td>
<td>414 (216-832)</td>
<td>359 (145-755)</td>
<td>95 (54-327)</td>
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<tr>
<td>Reinfection rate</td>
<td>7.8 (5.8-10.5)</td>
<td>8.0 (5.7-11.3)</td>
<td>9.6 (6.6-14.1)</td>
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<td>per 100py (95% CI)</td>
<td>15.5 (7.7-31.0)</td>
<td>23.2 (11.6-46.4)</td>
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<td>Second reinfection</td>
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<td>at last negative</td>
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<tr>
<td>HCV RNA PCR/first</td>
<td>22 (69)</td>
<td>19 (70)</td>
<td>3 (60)</td>
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<td>positive HCV RNA</td>
<td>1 (0)</td>
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<td>genotype (%)</td>
<td>2 (3)</td>
<td>1 (4)</td>
<td>1 (20)</td>
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<td>UNK</td>
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191 incident HCV infections

145 primary infections (negative HCV antibody prior to infection)
- 114 patients successfully treated for their primary infection
  - 27 reinfections
    - 13 reach SVR
      - 11 successfully treated
      - 2 spontaneous clearances
    - 6 reinfections
      - 3 spontaneous clearances
        - 1 reinfection (Treated successfully)
    - 1 reinfection (Treated successfully)
  - 31 patients spontaneously clear their primary infection
    - 5 reinfections
      - 4 reach SVR
        - 2 treated successfully
        - 2 spontaneous clearances
      - 1 spontaneous clearance
      - 1 reinfection (SVR pending)
  - 6 reinfections
    - 3 pending treatment outcome

46 with uncertain incident infection details
- Either spontaneously clear or successfully treated
  - 12 reinfections
    - 7 reach SVR
      - 4 successfully treated
      - 3 spontaneous clearances
    - 1 developed chronic HCV infection
    - 1 not treated
  - 2 failed treatment
  - 2 SVR pending
Definitions

• Reinfection:
  – Any newly positive HCV RNA PCR 24 weeks or more following end of treatment or clearance of the virus
  – Newly positive HCV RNA PCR within 24 weeks of end of treatment or clearance if reinfected with a different genotype

• Start of follow up:
  – Taken from end of treatment for individuals undergoing treatment
  – Taken as the mid-point between last positive PCR and first negative PCR result for spontaneous clearance

• Date of reinfection:
  – Mid-point between last negative HCV PCR result and first positive result
Definitions

Reinfection: Newly positive HCV RNA PCR within 24 weeks of end of treatment or clearance if reinfected with a different genotype.

Different genotype, treated incident infection

Same genotype, spontaneously cleared incident infection

Chelsea and Westminster Hospital
NHS Foundation Trust

SSAT
ST STEPHEN’S AIDS TRUST
British HIV Association
BHIVA

19th Annual Conference of the British HIV Association (BHIVA)

16–19 April 2013

Manchester Central Convention Complex