Treatment for hepatitis C infection in the UK Collaborative HIV cohort (UK CHIC) study

Alicia Thornton, Caroline Sabin, Sophie Jose, Sanjay Bhagani, David Chadwick, David Dunn, Martin Fisher, Richard Gilson, Janice Main, Alison Rodger, Chris Taylor, Mark Nelson
The aim of treatment for hepatitis C virus (HCV) is a sustained virological response (SVR): negative HCV-RNA 6 months after treatment has ceased.

SVR is associated with a reduction in the risk of liver-related events and it may reverse fibrosis and cirrhosis caused by HCV infection.

Treatment with Pegylated interferon (Peg-IFN) and ribavirin is long, difficult to tolerate and of low efficacy.

- 24.5% SVR among co-infected patients with genotype 1 or 4\(^1\)
- 59.4% SVR among co-infected patients with genotype 2 or 3\(^1\)

New treatment strategies (directly acting agents) are not yet available for everyone and regimens may still include Peg-IFN.

\(^1\) Davies et al, 2013, PLOS One
Aim:
- To describe patterns of treatment for HCV among a cohort of HIV/HCV co-infected individuals in the UK

Objectives:
1. To identify factors associated with receiving any HCV treatment
2. To characterise the treatment received with regard to drugs included and time on treatment
3. To identify factors associated with treatment failure defined as a positive HCV-RNA test in the one year after stopping treatment
UK CHIC

• Observational longitudinal study of HIV-positive adults
• 11 centres contributed additional data on HCV co-infected individuals seen for care from 2004 onwards including data on liver disease outcomes and HCV treatment

Inclusion/exclusion criteria

• All individuals included in the expanded data collection with a positive HCV-RNA test at any time during follow-up
• No evidence of HCV treatment before entry into the cohort
• Among treated individuals, at least one HCV RNA test in the year after stopping treatment
## Methods 2

- Cox proportional hazards models used to identify independent predictors of each outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Follow-up</th>
<th>Censoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Starting HCV treatment</td>
<td><strong>From</strong>: Earliest of cohort entry or first positive HCV test</td>
<td>Evidence of spontaneous HCV clearance</td>
</tr>
<tr>
<td></td>
<td><strong>Until</strong>: Starting treatment; date of death; last date of follow-up</td>
<td></td>
</tr>
<tr>
<td>2. Treatment failure</td>
<td><strong>From</strong>: Date of stopping treatment</td>
<td>Evidence of a subsequent course of HCV treatment</td>
</tr>
<tr>
<td></td>
<td><strong>Until</strong>: A positive HCV-RNA test; death; last date of follow-up</td>
<td></td>
</tr>
</tbody>
</table>
## Results: Treatment received

- 929/2272 (40.9%) co-infected individuals received any HCV treatment
- 114/929 (12.3%) received > one course of treatment

<table>
<thead>
<tr>
<th>Drugs included in regimen</th>
<th>1st episode of treatment</th>
<th>2nd episode of treatment</th>
<th>3rd episode of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg IFN/IFN alone</td>
<td>43 (4.6)</td>
<td>3 (2.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Peg IFN/IFN + Ribavirin</td>
<td>836 (90.0)</td>
<td>91 (79.8)</td>
<td>12 (85.7)</td>
</tr>
<tr>
<td>Regimens including DAAs(^1)</td>
<td>50 (5.4)</td>
<td>20 (17.5)</td>
<td>2 (14.3)</td>
</tr>
</tbody>
</table>

\(^1\)Regimens included: Peg-IFN and ribavirin plus either telaprevir or boceprevir; sofosbuvir plus ribavirin and sofosbuvir alone
Results: Individuals starting treatment

- 2163 individuals included in analysis, 820 of whom started treatment (37.9%):
  - Median age 37 (IQR 32, 43) years
  - 83.5% (1806/2163) of white ethnicity;
  - 61.1% (1322/2163) men who have sex with men (MSM)
  - 27.7% (601/2163) diagnosed with HCV in the acute stage

- Median time between first positive test and starting first HCV treatment: 11.2 months (IQR 3.7, 46.6 months)

- Median time on treatment: 47.7 (IQR 24, 48) weeks

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1 Excluding n=49 whose date of starting first episode of treatment was unknown; n=58 who started HCV treatment before their first recorded positive test; and n=2 individuals whose first treatment was before entry into the cohort
Results: Predictors of starting treatment

**Age** (per 10 years)

**Exposure**
- MSM
- IDU
- Male heterosexual
- Female heterosexual
- Other/Unknown

**Year first HCV positive**
- <1996
- 1997-1999
- 2000-2004
- 2005-2009
- >2010

**CD4 count** (per 100 cells/mm³)

**HIV viral load** (per log copies/ml)

**Acute HCV**
- Yes
- No

**Adjusted hazards ratio**
Results: Treatment failure

• Treatment episodes which included DAAs were excluded from the analysis

• There were 417 separate episodes of treatment where at least 1 HCV-RNA test result was recorded in the year after stopping treatment

• 138/417 (33.1%) episodes of treatment showed evidence of failure in the year after treatment ended

• No association was found between treatment failure and age, ethnicity, HIV exposure group, year of starting treatment, CD4 count, HIV viral load, HAART or treatment episode number
Results: Predictors of treatment failure

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Crude Odds ratio (95% CI)</th>
<th>P value</th>
<th>Adjusted Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute HCV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>-</td>
<td>1 (0.41-0.92)</td>
<td>0.01</td>
</tr>
<tr>
<td>Yes</td>
<td>0.70 (0.50-0.97)</td>
<td>0.03</td>
<td>0.61 (0.41-0.92)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>HCV viral load</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(per log copies/ml)</td>
<td>1.26 (1.04-1.53)</td>
<td>0.02</td>
<td>1.26 (1.12-1.42)</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>HCV genotype</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 or 4</td>
<td>1</td>
<td>-</td>
<td>1 (0.15-0.81)</td>
<td>0.01</td>
</tr>
<tr>
<td>2 or 3</td>
<td>0.42 (0.23-0.78)</td>
<td>0.01</td>
<td>0.34 (0.15-0.81)</td>
<td>0.01</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>1.32 (0.90-1.94)</td>
<td>0.15</td>
<td>1.67 (1.04-2.69)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>HBV co-infection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Yes</td>
<td>1.06 (0.65-1.73)</td>
<td>0.82</td>
<td>1.31 (0.74-2.31)</td>
<td>0.36</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.74 (1.10-2.75)</td>
<td>0.02</td>
<td>1.65 (0.85-3.30)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Time on treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(per week)</td>
<td>0.85 (0.78-0.92)</td>
<td>&lt;0.0001</td>
<td>0.73 (0.66-0.80)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

1 HCV viral load was unknown for 91 individuals
Limitations

- Limited post-treatment HCV-RNA test results
- Unable to assess end of treatment response or SVR
- Determining acute HCV infection
- No information on HCV reinfection
Summary and conclusions

- A significant group of co-infected individuals have not received treatment or have failed treatment for HCV infection.

- These individuals remain at risk of developing liver disease and would benefit from access to new treatment strategies:
  - In particular, those who are not diagnosed within the acute stage; those who with genotype 1 or 4 infection and those who remain on treatment for shorter period.

- Further work should concentrate on collection of data which can be used to assess treatment outcomes more thoroughly as new drugs become used more regularly.
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