Efficacy and safety of sofosbuvir/velpatasvir in people with chronic hepatitis C virus infection and recent injecting drug use: The SIMPLIFY study

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Background/rationale

- DAA therapy is effective in people receiving OST1-7 and people with a history of injecting drug use (including current/former people who inject)7-16
- Ongoing concern from some clinicians regarding DAA efficacy and risk of HCV reinfection among recent PWID
- In some settings in the US17-18 and Europe (Marshall, FRI Session O)19, DAA reimbursement restrictions are in place for recent PWID
- Recent PWID excluded from most HCV phase II/III protocols
- There are little data on DAA outcomes among recent PWID

SVR12 among former/recent PWID

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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12 (%)</td>
<td>96%</td>
<td>89%</td>
<td>95%</td>
<td>88%</td>
<td>87%</td>
<td>82%</td>
<td>95%</td>
<td>90%</td>
<td>86%</td>
</tr>
<tr>
<td>Number</td>
<td>44</td>
<td>89</td>
<td>93</td>
<td>215</td>
<td>60</td>
<td>59</td>
<td>142</td>
<td>88</td>
<td>971</td>
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</tbody>
</table>


SIMPLIFY: Study Design

- Investigator-initiated, Kirby/UNSW sponsored, international open-label trial
- 19 sites, 7 countries
- Study recruitment conducted through a network of drug and alcohol clinics (n=1), hospital clinics (n=12), and community clinics (n=2)
- Participants enrolled between April 2016 and October 2016
SIMPLIFY: Study Design

- DAA treatment-naïve patients with GT1-6 chronic HCV infection (F0-4)
- People with recent injecting drug use (past six months)
- Participants with HIV and decompensated liver disease excluded
- Electronic blister packs to monitor adherence

<table>
<thead>
<tr>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 24</th>
<th>3 yrs</th>
</tr>
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<td></td>
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Sofosbuvir/velpatasvir
400/100 mg od, n=103

SVR12
Six-monthly follow-up for reinfection

SIMPLIFY: Endpoints and statistical analysis

- SVR12 was the primary efficacy endpoint (intent-to-treat)
  - HCV RNA levels measured on local testing
  - Central testing with the Abbott RealTime HCV Viral Load assay (Abbott Molecular, lower limit of quantification of 12 IU/mL) is underway

- Adherence
  - Measured using an electronic blister-pack
  - Calculated by dividing the number of total doses received during therapy by the total expected number of doses

- Participants completed a self-administered questionnaire to collect information on demographics, drug and alcohol use, and injecting risk behaviours

- Detailed information on adverse events
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SOF/VEL (12 weeks)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>n=103</td>
</tr>
<tr>
<td>Age &lt;40 years</td>
<td>25 (24%)</td>
</tr>
<tr>
<td>Female sex</td>
<td>29 (28%)</td>
</tr>
<tr>
<td>Injecting drug use (in the last month)</td>
<td></td>
</tr>
<tr>
<td>No OST, no injecting</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>No OST, injecting</td>
<td>33 (32%)</td>
</tr>
<tr>
<td>OST, no injecting</td>
<td>15 (15%)</td>
</tr>
<tr>
<td>OST, injecting</td>
<td>43 (42%)</td>
</tr>
<tr>
<td>Injecting drug use (in the last month)</td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>57 (55%)</td>
</tr>
<tr>
<td>Methamphetamines</td>
<td>31 (30%)</td>
</tr>
<tr>
<td>Other opioids</td>
<td>22 (21%)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>13 (13%)</td>
</tr>
<tr>
<td>Daily injecting drug use (in the last month)</td>
<td></td>
</tr>
<tr>
<td>HCV genotype</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>36 (35)</td>
</tr>
<tr>
<td>2</td>
<td>5 (5)</td>
</tr>
<tr>
<td>3</td>
<td>60 (58)</td>
</tr>
<tr>
<td>4</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Fibrosis stage (METAVIR)</td>
<td></td>
</tr>
<tr>
<td>F0-F1</td>
<td>59 (62)</td>
</tr>
<tr>
<td>F2-F3</td>
<td>27 (28)</td>
</tr>
<tr>
<td>F4</td>
<td>9 (9)</td>
</tr>
</tbody>
</table>

SIMPLIFY: Participant disposition

- **Assessed for eligibility** (n=114)
- **Excluded** (n=11)
  - Lost to follow-up (n=3)
  - Patient refused (n=2)
  - HCV RNA negative (n=2)
  - Laboratory parameters (n=3)
  - Other, not specified (n=1)
- **Started treatment** Included in intention-to-treat analysis (n=103)
- **Did not complete treatment** (n=4)
  - Lost to follow-up (n=3)
  - Death due to overdose (n=1)
- **Completed treatment** (n=99)
- **Analysed** (n=103)
  - Efficacy: 103
  - Safety: 103
SIMPLIFY: SVR12

- 3 people lost to follow-up between ETR and SVR12 (no virological failure or viral relapse)
- 1 case of reinfection (1a-1a, % nucleotide: NS5A, 10.1%; NS5B, 4.6%, CoreE1, 12.0%)

SIMPLIFY: Impact of drug use and OST on SVR12

- No difference in SVR12 among people with (95%) and without recent injecting drug use (past month) at baseline (93%, P=0.683)
- No difference in SVR12 among people with (96%) and without recent ≥daily injecting drug use (past month) at baseline (93%, P=0.584)
- No difference in SVR12 among people receiving (93%) and not receiving OST at baseline (96%, P=0.598)
• Median adherence: 94%
• Mean adherence: 89%
HCV treatment and reinfection among active PWID

• Among recent PWID (past six months) with chronic HCV genotypes 1-4 treated with sofosbuvir and velpatasvir, SVR12 was 94%

• There was no impact of injecting drug use or OST at treatment initiation
  • Analyses are underway to evaluate the impact of on-treatment drug use

• There were no cases of virological failure or viral relapse, but one case of HCV reinfection was observed

• These data provide support for DAA HCV treatment among recent PWID

• Further studies are needed in people with more recent injecting and people with HCV/HIV co-infection

Acknowledgements

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