Treatment of Hepatitis C in People Who Inject Drugs (PWIDs)

Andrew Seaman, MD
OHA P&T Meeting
January, 2017
Conflicts of interest

- Receive <8% of my salary from an investigator initiated, Merck funded trial (makers of elbasvir/grazoprevir)

- I am highly influenced by the opinions, life experience, and knowledge my patients bring to the table (many of whom inject drugs)
Objectives

- Review of published and some unpublished data on PWIDs from colleagues in New York, Australia, Europe

- Brief review of the Old Town Clinic / Outside In / OHSU pilot trial for HCV treatment in People Who Inject Drugs
Alcohol use does not affect SVR12

C-EDGE CO-STAR Trial

- Multicenter-RCT tx w/ Elb-Graz with 301 PWIDs

- Patients with GT 1, 4, or 6 HCV on either methadone (81%) or buprenorphine (19%) for comorbid opioid use disorder

- Randomized 2:1 to immediate treatment group vs delayed treatment group (12wks placebo + 4 weeks de-randomization + 12 weeks treatment)

- Primary outcome SVR 12 assuming re-infection as cure

- Intention-to-treat analysis

### C-EDGE CO-STAR Trial

<table>
<thead>
<tr>
<th>Imm. Treat. Group (n=201)</th>
<th>SVR 12</th>
<th>SVR 24</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assuming Re-infections are Responses</strong></td>
<td>94% (89.8-96.9)</td>
<td>85% (78.8-89)</td>
</tr>
<tr>
<td><em>2/201 additional relapses</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Assuming Re-infections = Treatment Failure</strong></td>
<td>91.5% (CI 86.8-95%)</td>
<td>87%</td>
</tr>
<tr>
<td><strong>Probable Reinfection</strong></td>
<td>5/201</td>
<td>5/201</td>
</tr>
<tr>
<td><strong>Lost to Follow Up</strong></td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td><strong>Adherence &gt;95%</strong></td>
<td>~95%</td>
<td>95%</td>
</tr>
</tbody>
</table>

**2 year f/u re-infection data**

2.3/100pyrs

SIMPLIFY trial (pre-publication)

- Multicenter, international RCT with recent (<6mo) PWIDs
- 103 participants w/ GT 1-6 HCV
- Treated w/ Sof/Vel x 12 weeks
- Primary endpoint SVR12, secondary Adherence > 90%

Results

- 70% injecting in last month
- 57% receiving opioid substitution therapy
- End Treatment Response – 94% (NO confirmed VL failures – 6% loss to f/u)
- SVR12 and Adherence data pending
- Reinfection data pending (f/u 3 years)

Intensive management of HCV tx in PWIDs: Montefiore trial

Adherence higher in DOT vs. both Individual (p=0.0008) and Group (p=0.0003)

Window Daily Time Frame Adherence

Overall adherence: DOT (75.0%) vs. Group (61.4%) vs. Individual (62.4%)

SVR12 high in all 3 arms (p=0.24)

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>ETR</th>
<th>SVR12</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOT</td>
<td>98.0%</td>
<td>98.0% (50/51)</td>
</tr>
<tr>
<td>Group</td>
<td>93.8%</td>
<td>93.8% (45/48)</td>
</tr>
<tr>
<td>Individual</td>
<td>96.1%</td>
<td>90.2% (46/51)</td>
</tr>
<tr>
<td>Total</td>
<td>96.0%</td>
<td>94.0% (141/150)</td>
</tr>
</tbody>
</table>

PREVAIL study: Unpublished data from INHSU. LINK to slides.
OTC – OI – OHSU Pilot Study

- Prospective, non-randomized real world clinical trial using elb/graz to treat people who inject drugs with GT 1 or 4 HCV and an APRI <0.7 who:
  - Arm 1: engage with Medication Assisted Therapy (Methadone/Bupe), n=25, Old Town Clinic
  - Arm 2: are actively using and engage with needle exchange program, n=25, Outside In
  - Arm 3: matched cohort in OHSU hepatology clinic, n=50
Endpoints

- Primary
  - SVR 12 and 48

- Secondary
  - Primary Tx failure (+RNA 24wks)
  - Secondary Tx Failure (+RNA 60wks)
  - Adherence
  - Discontinuation rate
  - NS5a resistance
  - Substance use relapse
OHSU-OTC-OI Study Progress: Enrollment

- Old Town Clinic / MAT:
  - 25/25 enrolled
  - Adherence greater than 95% (All patients completed by Jan, SVR data by April 1)

- Outside In
  - 14/25 enrolled
  - Adherence good except 2/10 lost-to f/u (?) Sampling error

- OHSU
  - Pending
Limitations

- **Power**
  - Powered to detect a difference of 20% in primary endpoint; this is not clinically ideal

- **Group Disparities**
  - Comparing prospective trial w/ very specific inclusion criteria to chart biopsy based cohort
  - Difference in un-measurables between people in MAT program and needle exchange (and university setting)
  - Differences in pre-screening process
Old Town Clinic Treatment Program

- Multidisciplinary
  - Medical director + two providers
  - HCV coordinator
  - Clinical pharmacist
  - CADC

- Weekly committee meetings
  - Decision made on need for treatment candidacy, Substance Used Disorder support, adherence support
  - Drug, labs ordered and PA process started by coordinator
  - First, last, and SVR visit by provider, remainder by pharmacist
We treat... everyone

- **Treatment candidacy**
  - Made 2/3 last appointments or subjective adherence measure (whichever lower barrier)
  - Desires treatment
  - Meets their insurance eligibility criteria*

*We consider any SUDs support as treatment and have had great success with insurers*
Our capacity

- A total of 60 patients have initiated treatment in the last 9.5 months (24 study/36 non-study).
- We expect to treat many more in 2018.
Adherence

- Adherence has been near perfect in almost all cases.
- The 4 exceptions are: #1 ‘completed' 1 month interruption, #2 ‘discontinued’ completed 8 weeks, #3 ‘active’ 15 day interruption & #4 ‘active’ 24 day interruption.

Adherence - Not active

- Great Adherence (28)
- Adherence Issues (2)
Treatment efficacy

- Everyone that completed a SVR12 viral load has been undetectable.
Treatment as prevention depends on treating PWIDs

- Despite reinfection risk, not treating leads to a greater public health risk
- If we are not treating a patient population with at least some re-infection risk we are not treating the population that transmits this virus
- Multiple models suggest that we must treat PWIDs if we are to successfully address the HCV epidemic\textsuperscript{9,10}
In Summary: We can and must treat hep C in PWIDs

- There is no evidence of different hepatitis C treatment outcomes among people with or without substance use disorders
- The WHO and others recommend we prioritize rather than restrict treatment in PWIDs
- Mathematical models and common sense suggest we cannot treat this epidemic unless we treat the people transmitting the virus
- Where is the rational for denying people with substance use disorders?? The rational for “6 months sobriety?”
  - (Why not deny diabetics? People with metabolic syndrome? Tobaccoism?)
Questions?
References


