Is HCV Re-infection after DAA treatment an issue

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Background

• Oral DAAs cure >95% of those treated
  • WHO call for HCV elimination by 2030

• Treatment does not confer protective immunity
  • Reinfection possible after spontaneous or treatment induced clearance

• Highest risk groups for reinfection
  • People who inject drugs (PWID)
  • HIV infected men who have sex with men

• Reinfection a major challenge to HCV elimination
  • Major driver of provider and system level barriers to HCV treatment of high risk groups
  • Elimination dependent on reducing pool of individuals able to sustain epidemic through treatment and cure
High rates of HCV reinfection in high risk PWID

- 94 PWID enrolled from NSP, Dundee, UK
- Peg/IFN + RBV +/- Simeprevir/Telaprevir

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
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<tbody>
<tr>
<td>Age, mean (range)</td>
<td>34 (21-49)y</td>
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<tr>
<td>Male</td>
<td>67 (71)</td>
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<tr>
<td>Homeless</td>
<td>20 (21)</td>
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<tr>
<td>Current Opiate use</td>
<td>93 (99)</td>
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<td>Inject daily or more</td>
<td>51 (54)</td>
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<td>Harm reduction</td>
<td></td>
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<td>100% needle and syringe</td>
<td>75 (82)</td>
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<tr>
<td>OST</td>
<td>55 (63)</td>
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- Among 77 cured; 15/77 reinlected at 18mths
- Reinfection rate of 21.5/100PYs
- Age <30 associated with reinfection

7 year follow up of HCV cured PWID

HCV reinfection also associated with poor “social functioning”
Grebely et al Hepatology 2012

- 39% relapsed into IDU within 7 years
- Reinfection in 10 of 37 (27%) who relapsed vs 10 of 94 (11%) who did not
- Only predictor of reinfection was relapse
HCV reinfection among PWID in the oral DAA era

- British Columbia Hepatitis Testers Cohort
- Recent IDU <3 years (n=875) vs previous IDU > 3 years (n=1793) prior to SVR
- Reinfection rates in PWID
  - Recent 3.1/100 Pys
  - **Born after 1975 10.2/100Pys**
  - Previous 1.4/100Pys

Rossi et al J hepatology 2018
Impact of injection frequency on reinfection after oral DAA therapy

• Phase IV clinical trials (n=179)
  • SIMPLIFY & D3FEAT
  • 25 International sites
  • IDU <6 months or on OST
  • Treated with oral DAA 2016-17
  • Follow up to 2 years
  • No ongoing drug use: no reinfection
  • Ongoing drug use: Reinfection incidence 4.8/100Pys

Grebely et al ILC 2019
Increasing incidence of HCV infection among HIV positive MSM in the HAART era

HCV Incidence by risk group in the Swiss HIV Cohort Study

Wandeler et al. CID 2012
High rates of HCV reinfection among HIV positive MSM following SVR

**Interferon Era**
- HCV reinfection 3-10 x primary infection rate
- Reported HCV re-infection rates of 5.3-15.2/100 PYs
  - As many as 25-33% re-infected within 2 years
  - Multiple subsequent reinfections
  - Increasing re-infection rate with each subsequent re-infection
    - Eight centers in Europe
    - Re-infection rate
      - 7.3/100PYs 1\(^{st}\) reinfection
      - 18.8/100 PYs 2\(^{nd}\) reinfection

**Oral DAA era**
- Madrid co-infection registry (n=177)
  - Re-infection rate: 5.9/100PYs
- HIV infected MSM in NYC (n=305)
  - 1st reinfection 38/305 (12%)
    - Rate 4.4/100Pys (95% CI 3.1-6.0)
    - Median 1.9 yrs (IQR 1.3-3.6)
  - 2\(^{nd}\) reinfection 6/33 (18%)
    - Rate 8.7/100PYs (95% CI 3.5-18.1)
    - Median 1.1 yr (IQR 0.6-2.5) yrs

Drivers of HCV reinfection in MSM

Exact mechanism unknown

- HCV prevalence and incidence associated with
  - Receptive anal intercourse without a condom
  - Rectal trauma with bleeding
  - Group sex
  - Injection drug use
  - Chemsex-use of drugs to increase sexual disinhibition and arousal
    - Metamphetamine
    - Gamma hydroxybutyrate (GHB)

- Overlapping risk factors for HCV infection and reinfection in MSM

PWID

MSM
Modeling treatment as prevention and impact of reinfection in PWID

Rate of HCV reinfection following HCV treatment scale up assuming varying rates of HCV treatment

Required intervention to achieve 90% reduction in incidence

Martinello et al 2017 Cur HIV/AIDs report, Razavi INHSU 2015, Fraser et al Addiction 2018
Modeling impact of oral DAA on HCV Incidence among HIV infected MSM

HCV transmission model calibrated to France

HCV transmission model calibrated to Switzerland

Model Projection: By 2030
57% of all infections would be reinfections if risk behavior increases
23% will be reinfections if risk behavior stabilizes

Projected HCV prevalence over 10 years 2016-2026

Projected HCV incidence with different HCV treatment uptake and risk behavior scenarios

Modeling a short-term intensive intervention to interrupt HCV transmission in MSM with HIV

- Data from Swiss HIV Cohort Study
- Swiss HCVree trial
  - Active HCV testing of cohort
  - Patients with HCV genotype 1 and 4 offered treatment & risk counselling
  - Risk counselling behavioral intervention at 4, 6, 8 and 12 weeks

Salazar-Vizcaya JVH 2018
Addressing the challenge

• HCV elimination requires improved engagement with populations at highest risk of sustaining the epidemic
• Reinfection should be viewed as a sign of this engagement
• In the absence of an effective HCV vaccine, the HCV care continuum does not end with cure
• Efforts to prevent, detect and promptly retreat reinfection a priority

Falade-Nwulia et al JVH 2018
Surveillance is key to early detection, retreatment & enhanced behavioral intervention

HCV Reinfecion

Recurrence of HCV viremia (novel genotype/subtype)
Recurrence of HCV viremia (any genotype/subtype)

Treatment initiation
End of treatment
SVR 12

A proposed clinical definition for HCV reinfection when the gold standard of phylogenetic analysis of pre- and post-treatment HCV sequences are not available

Falade-Nwulia et al JVH 2018
What will be required to limit impact of HCV reinfection

- Combination interventions
- Opioid substitution therapy
- High coverage NSP
- Integrated care
  - Mental health
  - Case management for linkage to housing, job programs etc
  - Peer based programs to support abstinence and safer injection
- Behavioral interventions for safer injection
- Education-Counseling and peer support
- Counselling on safer sex
  - Consistent condom use
  - Avoiding drug use with sex
- Drug use screening, brief intervention and referral for treatment
- Linkage to harm reduction
- Regular post treatment surveillance (HCV RNA) and retreatment

Contextual
- Network based treatment e.g TAP trial
- Destigmatization
- Effective HCV vaccine

Falade-Nwulia et al JVH 2018
Summary

• Treating HCV in groups with the highest burden/risk is critical to HCV control at the population level
• HCV reinfection is a challenge to HCV elimination that can be addressed
• Will require acceptance of reinfection as a marker of treatment of high risk populations
• The HCV care continuum needs to be extended beyond cure; counsel on monitor for and promptly treat reinfection. More data needed.
• Need for development and evaluation of strategies to optimize HCV treatment uptake, integrate harm-reduction strategies and other wrap around services for prevention of HCV reinfection.
• Effective behavioral interventions are needed to further address reinfection risk in the highest risk groups
Thank you
Questions