HCV/HIV among People who Inject Drugs

What Issues Remain?

INSHU 2017

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Disclosures

- Salary support: les FRQ-S “Chercheur National” Career award
- Grant support: CIHR, CIHR-CTN, NIH, FRQ-S
- Research grants for investigator initiated trials: ViiV, Merck
- Consulting fees: ViiV, BMS, Merck, Gilead
What issues DON’T Remain

Efficacy of treatment

The Hepatitis C Treatment Revolution

2015 AASLD/IDSA Guidance: “HIV/HCV co-infection should receive the same treatment as recommended for HCV mono-infection”
Next Generation Direct-Acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

Coformulated: G/P

In vitro:\(^1,2\)
- High barrier to resistance
- Potent against common NS3 polymorphisms (e.g., positions 80, 155, and 168) and NS5A polymorphisms (e.g., positions 28, 30, 31 and 93)
- Synergistic antiviral activity

Clinical PK & metabolism:
- Once-daily oral dosing with food
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg
Glecaprevir was identified by AbbVie and Enanta.


EXPEDITION-2 Study Design

A phase 3, multicenter global study evaluating 8- or 12-week treatment with G/P in HCV/HIV-1 co-infected adults without or with compensated cirrhosis, respectively

Patients were enrolled in Australia, Belarus, France, Germany, Poland, Puerto Rico, Russian Federation, United Kingdom and United States

EXPEDITION-2: Safety and Efficacy of Glecaprevir/Pibrentasvir in HCV Genotype 1-6-infected Patients Coinfected with HIV-1 | IAS | 24 July 2017

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.
Efficacy

- One patient with GT3 infection and cirrhosis had on-treatment virologic failure at week 8; the patient was 85% compliant with treatment
- Tx combined with integrase inhibitors, ripivirine, boosted darunavir and lopinavir (in non-cirrhotics)

*Patient returned at post-treatment week 24 and had achieved SVR

**EXPEDITION 2: Safety and Efficacy of Glecaprevir/Pibrentasvir in HCV Genotype 1-6-infected Patients Coinfected with HIV-1 | IAS | 24 July 2017**

The Canadian Coinfection Cohort
2003-2016 (n=1695)
Clinical Trials in Co-infection

Phase 3 Trials evaluating 2nd generation DAAs in co-infected individuals

Using PubMed & clinicaltrials.gov
As of September 2015
Rapid scale up of HCV treatment since DAAs

Real world SVR rates excellent across risk groups

What issues do remain?

Co-management and DRUG-DRUG interactions
Challenges of dual infection

1. Complicating comorbid medical and mental health conditions
2. Lower access to HIV and HCV care
3. Lower adherence to therapy
4. Medication side effects and toxicities
5. Concomitant substance use treatment
6. Drug interactions

Therapeutic failure generally correlates with the degree that drug use disrupts daily activities rather than with drug use per se

Drug-Drug Interactions: DAAs

See also http://www.hep-druginteractions.org/

DRUG-DRUG interactions: Street drugs & OST

- MDMA, GHB, ketamine, and methamphetamine all have the potential to interact with ARV agents because all are metabolized by the CYP450 system.
- Overdoses secondary to interactions between MDMA or GHB and PI-based ART have been reported.
- Because of its opioid-induced effects on gastric emptying and the metabolism of CYP450 isoenzymes 2B6, 3A4, and 2D6, pharmacologic effects and interactions between methadone with ARV agents may commonly occur.
  - may diminish the effectiveness of either or both therapies by causing opioid withdrawal or overdose, increased methadone toxicity, and/or decreased ARV efficacy but no major issues with DAAs.
- Limited information is currently available about interactions between buprenorphine and ARV agents and appears safe with DAAs.
- Naltrexone not expected to have major interactions.

What issues do remain?

It’s a matter of risks and vulnerabilities.
Global prevalence of HCV in HIV+ persons

HCV — 20% diagnosed, yet major Tx gap; cost reductions < $150 / cure

Sources — WHO, work conducted by Center for Disease Analysis

Gottfried Hirnschall
HCV Care Cascade Canada

> 90% diagnosed among HIV+

Main barrier to HCV elimination in HIV-HCV coinfection: Treatment uptake
Injection of prescription opioids: a significant threat to HIV and HCV prevention among PWID

Association between frequent injection (≥120/month) and drugs injected in the month prior to interview (N=2829 visits).

<table>
<thead>
<tr>
<th>Drugs category</th>
<th>No.</th>
<th>%</th>
<th>Crude PR</th>
<th>Adjusted PR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crack/cocaine ± other drugs</td>
<td>1008</td>
<td>35.6</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Prescription opioids only</td>
<td>422</td>
<td>14.9</td>
<td>2.93</td>
<td>2.84 (2.14-3.77) **</td>
</tr>
<tr>
<td>Prescription opioids + heroin/speedball, crack/cocaine or other drugs</td>
<td>1176</td>
<td>41.6</td>
<td>4.13</td>
<td>3.73 (2.94-4.73) **</td>
</tr>
<tr>
<td>Heroin/speedball ± crack/cocaine or other drugs</td>
<td>207</td>
<td>7.3</td>
<td>1.74</td>
<td>1.73 (1.20-2.50) *</td>
</tr>
<tr>
<td>Other drugs only</td>
<td>16</td>
<td>0.6</td>
<td>0.55</td>
<td>0.51 (0.07-3.48)</td>
</tr>
</tbody>
</table>

Abreviations: PR: prevalence ratio; CI, confidence interval; Ref, reference.
** p<0.0001; * p<0.01.


E. Roy¹,², P. Leclerc³, C. Morissette³, C. Blanchette⁴, K. Blouin⁵, N. Arruda¹, M. Alary⁶ IAS 2017
An emerging epidemic

Figure 8: HIV Cases by Selected Self-reported Ethnicity in Saskatchewan, 2000 to 2009.

HIV Rates by Population

3.5% Ahtahkakoop

3.76% Austin, Indiana

Source: Public Health Agency of Canada
Centers for Disease Control and Prevention (CDC)
Barriers to HCV Treatment

**Structural Barriers**
- Lack of infrastructure/multidisciplinary support
- Segregated services
- Provincial regulations
- Cost

**Provider Barriers**
- Poor awareness/education
- Reticence to treat IDUs
- Lack of providers, especially in remote communities
- Focus on HIV

**Patient Barriers**
- Poor awareness/education
- Lack of symptoms
- Competing health priorities (HIV, psychiatric)
- Competing social priorities (housing, substance use, financial, food insecurity)
- Fear of side effects
Hepatitis C virus infection incidence rates by transmission group


Updated from Wandeler G et al. SMW 2015

Andri Rauch, SHCS

www.iasociety.org

The international love life of the Swiss

Salazar-Vitzaya et al. IWHOD 2017

Andri Rauch, SHCS

www.iasociety.org
The main factors that have influenced and define ChemSex behaviour have been:

- The increased availability and use of three recreational drugs by MSM in London, including crystal methamphetamine, methedrone, and PrEP
- Increased injecting use of crystal methamphetamine and methedrone by MSM. Traditionally, MSM have preferred drugs like ecstasy and "naive" injection practices
- The use of smartphone Apps and online 'hooking-up' sites to seek sexual activity as well as procuring drugs. While some

Dean Street MSM ChemSex Presentations (>500) Key learnings:
- Good understanding about HIV transmission risks, prevention strategies and comfort with disclosure of serostatus, viral load
- Serosorting common
- HCV however much more stigmatizing, less likely to be disclosed and common reason for rejection online
- Reluctance to disclose high risk practices and drug use
- "Naive" injection practices
What issues do remain?

Implications for elimination

<table>
<thead>
<tr>
<th>Slang, street name, colloquial terms</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>Tina/Meth/hop/Crystal</td>
<td>Crystal methamphetamine, which can be injected, smoked, snorted or orally</td>
</tr>
<tr>
<td>Meph/Meow Meow/Drone</td>
<td>Mephedrone, which can be snorted, injected, swallowed or orally</td>
</tr>
<tr>
<td>G/Gika</td>
<td>(GHB/GBL, taken orally or by injection)</td>
</tr>
<tr>
<td>Slamming/Slammed/to slam</td>
<td>Injecting/injected/oral use of drugs</td>
</tr>
<tr>
<td>Barebacking</td>
<td>Condomless anal intercourse</td>
</tr>
<tr>
<td>Booty-bumping</td>
<td>To squirt diluted drugs into the anus</td>
</tr>
<tr>
<td>Bender</td>
<td>Episode of drug use</td>
</tr>
<tr>
<td>Chemix</td>
<td>Recreational drugs</td>
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</tbody>
</table>

**Associated with**

Extended sex for many hours/several days.
More extreme sexual practices/traumatic sex
Multiple partners
Extreme sexual disinhibition/extreme sexual focus
Unpredictable drug interactions (e.g., GHB & alcohol)
Increased injecting use amongst an injecting-naive population; BBV risks & injecting-related harms
Poor condom use
Poor ARV adherence
Frequent STIs (including a current Shigella outbreak); HIV infections, HCV infection/repeated re-infections
Multiple and repeated use of PEP
Psychosis/ physical dependence/ overdoses
**Risk behavior and treatment-as-prevention**

**A. Further increase in high-risk behavior**

- Current treatment uptake (0.22/yr)
- Increased treatment uptake (1/yr)

**B. Stabilization in high-risk behavior**

- Current treatment uptake (0.22/yr)
- Increased treatment uptake (1/yr)

WHO target: -90%

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**BERLIN: INCREASING INCIDENCE AND HIGH TESTING/TREATMENT, NEED ACUTE TREATMENT OR BEHAVIOR CHANGE**

Difficult to reverse increasing incidence with existing high testing/treatment rates.
Requires:
- All newly diagnosed treated within 3 months (licensing for acute treatment), or
- All newly diagnosed treated within 6 months plus 10% risk behavior reduction

90% reduction

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Martin NK and Ingiliz P, preliminary work
The Dutch experience

HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Best estimate of road to HCV elimination in HIV+ patients in The Netherlands:
- 76–83% cured of HCV
- 17–24% still to be cured of HCV

Acute HCV infections in 2014 and 2016

IRR 0.49
(95% CI 0.34–0.69)

Discussion

Acute HCV problem is still far from being ‘eliminated’!
Reduction seems to stabilise in 2017 (IRR 0.5 in Jan-Apr 2017)

- Cross-border and cross continent transmission
  - Most new infections in Amsterdam area
- Undiagnosed HCV among HIV+ MSM: even in resource-rich setting
- Undiagnosed HCV among HIV- MSM: pool for re-introduction in HIV+
  - 4.8% prevalence of chronic HCV at time of PrEP initiation in Amsterdam
  - N=8/13 were using PREP at time of HCV infection
- DAAs unapproved for acute HCV => ongoing transmission during wait

DAAs for all HIV+ patients with chronic HCV will not suffice to ‘eliminate’ HCV

(1) E Hoornenburg et al. AIDS 2017
Are co-infected at increased risk of reinfection?

Risk behaviours after SVR

Injection Drug Use

Alcohol consumption

Mortality causes by birth cohort and HCV status

Man Wah Yeung et al HIV Clin Trials 2015
Do DAAs reduce mortality?

- Beware of Competing risks: How HCV and HCV treatment tie overall into drug user health?

Kronfli, IAS 2017

Early impact of DAAs in co-infection

Kronfli IAS 2017 and submitted
Sustained virologic response (SVR) after hepatitis C virus (HCV) treatment does not lead to improved renal function in HIV/HCV coinfected patients

Carmine Rossit, Erica E. Moodiet, Mark Hultt, Valerie Martel-Lafayette, Marie-Louise Vachon, Curtis Coopert, Neora Picket, Sharon Waldsley, and Marina B. Klein for the Canadian Co-Infection Cohort Study Investigators

Table 2: Association between SVR and annual rates of change in eGFR in the PS-matched sample (n=996)

<table>
<thead>
<tr>
<th></th>
<th>ΔeGFR (mL/min/1.73m² per year) (95% CI)</th>
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<tbody>
<tr>
<td>SVR</td>
<td>-1.21 (-1.69, -0.74)</td>
</tr>
<tr>
<td>Chronic Infection</td>
<td>-1.28 (-1.69, -0.86)</td>
</tr>
<tr>
<td>Difference</td>
<td>0.06 (-0.57, 0.69)</td>
</tr>
</tbody>
</table>

And finally .... what remains
Multidisciplinary Approach

HIV/HCV treatment team
MDs/Nurse/pharmacist

- Adherence HIV & HCV Rx
- Manage DDIs
- Manage comorbidities
- Ongoing surveillance for HCC

Peer and social support

- Food security
- Housing
- Culturally competent care and supports

Mental Health and Addictions

- Harm reduction
- ChemSex counselling
- Alcohol
- Smoking cessation

THANKS!