Micro-elimination
HIV/HCV Co-infection

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Learning objectives

- The role of microelimination
- Considerations for HIV/HCV co-infection
Viral hepatitis is a leading cause of death worldwide.

HCV account for 50% mortality

Source: WHO Global Health Estimates
Mortality due to cirrhosis and hepatocellular carcinoma is increasing

**FIGURE 1** Deaths from viral hepatitis, by virus and type of sequelae, 2013 (1)

- **HAV**: hepatitis A virus; **HBV**: hepatitis B virus; **HCC**: hepatocellular carcinoma; **HCV**: hepatitis C virus; **HEV**: hepatitis E virus.

WHO, 2016,
Combating Hepatitis B and C to reach elimination by 2030
Elimination of the cause can improve clinical outcomes

- **Chronic injury**
  - Viral infection
  - Alcohol
  - NASH
  - Autoimmune disorders
  - Cholestatic disorders
  - Metabolic diseases

- **Genetic polymorphisms**
  - Epigenetic marks
  - Cofactors (such as obesity and alcohol)

5–50 years

- **Liver failure**
- **Portal hypertension**

- **Liver transplant**

- **Cirrhosis**
  - Disrupted architecture
  - Loss of function
  - Aberrant hepatocyte regeneration

- **Hepatocellular carcinoma**

- **Regression**
  - Removal of underlying cause
  - Anti-fibrotic drug or cell therapy

- **Resolution**

- **Early fibrosis**
  - Inflammatory damage
  - Matrix deposition
  - Parenchymal cell death
  - Angiogenesis

- **Normal liver**

Pellicoro et al. Nature Reviews 2014
Elimination of hepatitis as a public health threat

80% of eligible patients treated for HBV and HCV by 2030

WHO, 2016, Combating Hepatitis B and C to reach elimination by 2030
Are the HCV targets even feasible?

<table>
<thead>
<tr>
<th></th>
<th>GP risk</th>
<th>PWID risk</th>
<th>Treatment</th>
<th>Access</th>
<th>% Diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basecase</td>
<td>As in 2015</td>
<td>As in 2015</td>
<td>PEG-IFN+RBV</td>
<td>As in 2015</td>
<td>As in 2015</td>
</tr>
<tr>
<td>+ Blood / injection safety</td>
<td>80% reduction</td>
<td>80% reduction</td>
<td>50% coverage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ PWID harm reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ DAAs as treat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ DAAs at diag.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Proactive diag.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>90% by 2030</td>
</tr>
</tbody>
</table>

Heffernan, Lancet 2019
No DAA and status quo scenarios

Blood safety and IPC interventions reduce mortality in long term

PWID harm reduction or DAAs at the time of diagnosis improves long term outlook

Ambitious diagnosis and treatment scale-up: WHO elimination - 65% reduction by 2034

Heffernan, Lancet 2019
But elimination is a huge and complex target...

- In 2017, EASL suggested to grapple with the HCV elimination challenge by setting micro-elimination goals

‘Obstacles to reaching this goal can best be overcome through a micro-elimination approach’
Micro-elimination

Pursuing elimination goals in discrete populations through multi-stakeholder initiatives

Helps tailor interventions to the needs of these populations.

Allows for quick, efficient targeting of treatment and prevention services.

Lazarus et al JHep 2017; Sem Liver Dis 2018
Suitable populations

• Patients with advanced liver disease
• Haemophilia patients
• Prisoners
• Children
• Patients engaged with drug treatment units
• Migrant communities from high prevalence regions*
• People who inject drugs in networks*
• Men who have sex with men
• Generational cohorts of high prevalence
• Geographically defined areas
• PLWHIV
HIV/HCV co-infection

- Around 2.3 million patients with HCV are co-infected with HIV.
- New HCV infections are increasing in HIV+ MSM population in Europe.
- Current incidence may be as high as 1-2% persons year of follow-up.
- High rates of acute HCV has been observed in HIV+ MSM in many European countries, US and Australia.
- Treatment response, SVR rates are similar to HIV non-infected population with DAAs.

Hullegie et al. CMI 2015; Wandeler et al. CID 2012
Risk of acute HCV infection

MSM > Heterosexual transmission

ECDC Report 2017
High rates of acute HCV infection/re-infection in HIV+ MSM

HIV+ MSM are at >20x higher risk of re-infection compared to initial infection rates

This is attributed to mucosally-traumatic sex

High use of methamphetamine

IVDU before or during sex (also called slamming or “slamsex”) is another significant risk factor for HCV transmission

Schmidt et al. PLoS One 2011; Ramière et al. CID 2019
Other factors contributing to high rates of acute HCV and re-infection rates

- Rectal shedding of HCV in HIV-coinfected MSM
- Transmission of HCV from dendritic cells
- High prevalence of chronic – underlying untreated population
- Mainly due to restrictions in DAA treatment in many countries

Foster et al. CID 2017; Nijmeijer et al. JIAS 2019
Spontaneous clearance in HIV population

- SC occurs rarely
- Approximately among 10-15% of patients
- Approximately 90% develop chronic disease
- <2 log10 drop is a strong predictor of chronic infection

Chromy et al. UEGJ 2019; Boesecke et al. CROI 2018
Could we use treatment as prevention to avert new HCV infections?
51% decrease in acute HCV infections among HIV+ MSM in Dutch cohort

Boerekamps et al. CID 2018
49% reduction in incident HCV infection in Swiss cohort

Braun et al. CID 18
68% reduction (all) and 79% reduction (first) acute HCV in London cohort

Garvey et al. CROI 2019
HIV and HCV co-infection also brings opportunities

- Widely available testing and treatment
- Mechanisms in place for monitoring progress
- Patient group engaged in care
Scale up of testing and treatment
Treatment of HCV in HIV/HCV

Every person with HCV/HIV co-infection must be considered for DAA-based anti-HCV treatment regardless of liver fibrosis stage.

Treatment indication and regimens are to be the same as in HCV mono-infection.

Re-test for GT and sub-type should be performed in persons with tests carried out before second-generation tests were available or in persons at risk of ‘super-infection’
Case study

• 35 year old MSM
• HIV+ on EFV/FTC/TDF, stable on ARVs
• Recently treated for syphilis
• Admits to having chemsex
• Counselling provided

• 3 months later he has LFT elevation
• HCV RNA >1 million copies/ml

• Do we treat? When do we treat?
Algorithm for management of acute HCV

EACS Guidelines, 2018

- Repeat HCV RNA Week 4
  - HCV RNA-positive < 2*log_{10} reduction in VL
  - HCV RNA-negative positive
    - a) Treat with short duration DAAs
    - b) Enrol in clinical trial for acute HCV treatment
  - HCV RNA-negative
    - Repeat HCV RNA at 24 weeks and 48 weeks to confirm spontaneous clearance
- Confirmed diagnosis of acute HCV
  - Risk reduction programme
  - Early treatment of concomitant STI, see page 67
Case study

Provided counselling

Risk reduction strategies

4 weeks later, HCV RNA less than 2log 10 drop

You decide to treat him

HCV Gt 3, non-cirrhotic
IFN-containing HCV regimens are no longer recommended

First generation HCV PIs (boceprevir and telaprevir; only indicated in GT1) are no longer recommended

Due to drug-drug interactions in particular HIV and HCV PIs careful checking for interactions is recommended prior to starting HCV therapy
What does the guidelines recommend?

<table>
<thead>
<tr>
<th>HCV GT</th>
<th>Treatment regimen</th>
<th>Treatment duration &amp; RBV usage</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Non-cirrhotic</td>
</tr>
<tr>
<td>3</td>
<td>GLE/PIB</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF/VEL +/- RBV</td>
<td>12 weeks +/- RBV or 24 weeks without RBV</td>
</tr>
<tr>
<td></td>
<td>SOF + DCV +/- RBV</td>
<td>12 weeks +/- RBV or 24 weeks without RBV</td>
</tr>
<tr>
<td></td>
<td>SOF/VEL/VOX</td>
<td>8 weeks</td>
</tr>
</tbody>
</table>
## Drug-drug interactions

| HCV drugs            | ATV/c | ATV/r | DRV/c | DRV/r | LPV/r | EFV | ETV | NVP | RPV | MVC | BIC | DTG | EVG/c | RAL | ABC | FTC | 3TC | TAF | TDF |
|----------------------|-------|-------|-------|-------|-------|-----|-----|-----|-----|-----|-----|-----|------|------|-----|-----|-----|-----|-----|-----|
| daclatasvir          | ↑     | ↑     | ↑     | ↑     | ↑     | ↓32 |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | ↑10% E10% |
| elbasvir/             | ↑     | ↑     | ↑     | ↑     | ↑     |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | ↓7/14% E34% |
| grazoprevir          | ↑     | ↑     | ↑     | ↑     | ↑     | ↓54/83 |     |     |     |     |     |     |     | ↑    |     |     |     |     |     |     |
| glecaprevir/pibrentasvir | ↑   | ↑553/64% | ↑ | ↑397%/- | ↑338/146% |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | E29% |
| paritaprevir/ombitasvir/ | ↑ | ↑94%i | ↑ | D-vi | ↑     |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     |     |
| dasabuvir            | ↑     | ↑     | ↑     | ↑     | ↑     |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     |     |
| simeprevir           | ↑     | ↑     | ↑     | ↑     | ↑     | ↓71% |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | ↓11% E8% |
| sofosbuvir/ledipasvir | ↑vii | ↑18/113%viii | ↑viii | ↑34/39%viii |     |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | D=20% E32% Evi |
| sofosbuvir/velpatasvir |     | ↑/-142%viii |     | ↓28%/-vii | ↓29%/-viii |     |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | Evi |
| sofosbuvir/velpatasvir/voxilaprevir | ↑ | ↑40/93/331%vii | ↑ | ↑/- | ↑-|/143%vii |     |     |     |     |     |     |     | ↑    |     |     |     |     |     | E Evi |
| sofosbuvir          |     |     | ↑34% |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

**Legend:**
- ↑: Increase
- ↓: Decrease
- E: Equal
- D: Decrease
- vi: vi
- vii: vii
- viii: viii

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Drug drug interactions

• https://www.hep-druginteractions.org
Case study

Switched ARVs to DTG/ABC/3TC

Received 8 weeks DAAs (Grazoprevir/elbasvir)

SVR achieved 6 months later with re-infection...
Challenges remaining

Reinfection remains high
Ongoing need to promote risk reduction
Design screening policies

Setting up micro-elimination targets
Wider and cheaper DAA availability is required
THANK YOU