Dogma: HCV treatment for eradication

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Disclosures

• Some discussion of non-HC approved compounds
• Industry:
  – AbbVie
  – Gilead
• Academic:
  – Affiliation with Dalhousie University and Nova Scotia Health Authority
• Advocacy:
  – HIV and HCV patient advocacy groups
Objectives

- Describe an infectious disease plan for the elimination of HCV

- Contrast current oral HCV treatment options, including duration and cure rates

- Predict which key populations should be treated to facilitate elimination
Infectious diseases and eradication
Traditional characteristics for infectious disease eradication

- Low $R_o$
  - Difficult to / not easily spread
  - Susceptibility and protection
    - Naturally induced immunity
    - Vaccine
- Declining prevalence naturally
- Easily diagnosed
- Exposure to symptom time is short
- No animal reservoir
Traditional characteristics Eradication and HCV

- $R_0 \sim 2$
- No vaccine
- Reinfetction possible
- Incidence $\uparrow$
- Reliably curable
- Clinically indolent BUT easily identified if tested
- Long exposure-to-symptom time
- No animal reservoir
- Discrete human reservoir
Traditional characteristics

Eradication and HCV

- $R_0 \approx 2$
- No vaccine
- Reinfeciton possible
- Incidence ?
- Reliably curable
- Clinically indolent
- BUT easily identified if tested
- Long exposure-to-symptom time
- No animal reservoir
- Discrete human reservoir
Screening challenges
Eradication and HCV: Treatment for cure

- $R_0 \sim 2$
- No vaccine
- Reinfection possible
- Incidence?
- Clinically indolent but easily identified if tested
- Long exposure-to-symptom time
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Ideal HCV treatment

Highly efficacious (cure for all treated)
All oral
No/low side effects
Short
Once daily

Accessible
HCV: the direct acting antiviral revolution
Protease inhibitors
e.g. simeprevir, paritaprevir

Direct acting antivirals

NS5A inhibitors
(e.g. ledipasvir, ombitasvir)
AND
Polymerase inhibitors
(e.g. sofosbuvir, dasabuvir)

New HCV regimens

Cure (%)

- IFN RBV
- 1st gen protease inhibitors IFN/RBV
- QUEST1 & 2 Simeprevir IFN/RBV Rx naive
- ASPIRE Simeprevir IFN/RBV Rx exp
- LONESTAR-2 Sofosbuvir Rx exp SHORT GT 2,3
- COSMOS Sof + Sim SHORT GT1
- SAPPHIRE I and II 4 drug Rx exp and naive SHORT GT1
- PEARL IV 3 or 4 drug Rx naive SHORT GT1
- PEARL III 3 or 4 drug Rx naive SHORT GT1a
- TURQUOISE II 4 drug Rx exp / naive SHORT GT1 With cirrhotics
<table>
<thead>
<tr>
<th>HCV genotype</th>
<th>Sofosbuvir</th>
<th>Sofosbuvir/ledipasvir</th>
<th>Simeprevir</th>
<th>PRV/r/OMV/DSV (RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>X (with PEG-IFN/RBV)</td>
<td>X</td>
<td>X (with PEG-IFN/RBV)</td>
<td>X</td>
</tr>
<tr>
<td>1b</td>
<td>X (with PEG-IFN/RBV)</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>2</td>
<td>X (with RBV)</td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td>X (with RBV)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>X (with PEG-IFN/RBV)</td>
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Pre-approval: Daclatasvir* in HIV/HCV coinfection

<table>
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<th>Naive</th>
<th>Experienced</th>
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<tbody>
<tr>
<td>Randomize 2:1</td>
<td>50</td>
</tr>
<tr>
<td>101</td>
<td>52</td>
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</tbody>
</table>

N = 203

DCV 30/60/90 mg + SOF 400 mg QD

GT 1 (N = 168)

SVR12, %

100

12-Week Naive

90

12-Week Experienced

80

8-Week Naive

70

* Not yet Health Canada approved

Wyles et al. CROI 2015 Seattle WA
Pre-approval:
Grazoprevir*, elbasvir* and riba in HCV genotype 1

HCV GT1
n=253 pts
Treatment naïve and exp
Cirrhotic and non-cirrhotic

* Not yet Health Canada approved

Lawitz et al. 2015 Lancet 385; 1075
New HCV regimens: Key points

Highly efficacious (greater than 90% cure)
All oral
No/low side effects
Short (12 weeks currently, ?shorter)
Low pill burden (1 pill–8 pills/day)

Accessible
R₀ ~ 2

No vaccine

Clinically indolent
BUT easily identified if tested

Long exposure-to-symptom time

No animal reservoir

Reliably curable

Reinfection possible

Incidence ?

Discrete human reservoir
Treatment as prevention in ‘transmitters’: what have we learned in TB

Gallant et al. Canadian communicable diseases report vol 40-6: Mar. 20 2014
Treatment as prevention in ‘transmitters’: what have we learned in HIV

Treatment as prevention in ‘transmitters’: what about HCV?

Hellard et al. 2014 Hepatology 60: 1861
Treatment as prevention in ‘transmitters’: what about HCV?

• Treatment as prevention with new DAAs will probably work at the population level for high risk individuals to prevent transmission….but we don’t know

• Pilot studies to look at HCV reinfection and its mechanisms (behavioral and immune) are needed
Treatment for elimination

treatment for prevention

\[ R_0 \approx 2 \]

No vaccine

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BUT
easily identified if tested

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Treatment for elimination
treatment for prevention

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HCV infection: decreased prevalence and incidence through treatment and care
HCV infection: decreased prevalence and incidence through treatment and care

Canadian estimate

HCV
220,000-250,000

Identify the reservoir

Treatment of the human reservoir

Treat those with high risk for reinfection

Reduce reinfection risk

Elimination

Trubnikov M, Yan P, Archibald C.
Canada Communicable Disease Report:
Volume 40-19
**Answering the challenge: principles for HCV eradication**

<table>
<thead>
<tr>
<th>Care providers committed to education and HCV care</th>
<th>Engagement of the persons living with HCV community</th>
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<tr>
<td>Industry and government partnership to access treatment</td>
<td>Practical and pragmatic evaluation and investigation that promotes ongoing improvement</td>
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9. Set targets for national disease elimination with a comprehensive monitoring and evaluation plan to assess progress
You don’t have to see the whole staircase, just take the first step.

Martin Luther King, Jr.

VISION
A world without HCV

GOAL
Elimination of HCV
Through treatment? And treatment as prevention? And a vaccine?