Models of HCV elimination in co-infected patients in The Netherlands

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Conflicts of interest

Durex sponsors all my one-night stands.

(Drawing by Vamagurka)
Conflicts of interest

- **Within the context of the presentation:**
  - Research grant from Merck Sharp & Dohme (ongoing, 2014–17)

- **Outside the context of this presentation:**
  - Research grants from Gilead Sciences (ongoing, 2013–17)
  - Investigator of trials sponsored by Merck Sharp & Dohme, Gilead Sciences, Janssen-Cilag
  - Invited speaker: Gilead Sciences, Merck Sharp & Dohme, Pfizer, Janssen-Cilag
  - Advisory board participation: Bristol-Myers Squibb, AbbVie, Merck Sharp & Dohme, Gilead Sciences, Janssen-Cilag
  - Conference invitation: Bristol-Myers Squibb, AbbVie, Merck Sharp & Dohme, Gilead Sciences, Janssen-Cilag
  - Consultancy: GL pharmaceuticals
HCV in HIV+ men who have sex with men (MSM) in The Netherlands
The HIV/HCV co-infected population in The Netherlands is well known

The ATHENA cohort

- 26 HIV treatment centres recognised by the Ministry of Health
- Collection of pseudonymised demographic and clinical data by Stichting HIV Monitoring (SHM)
- As of May 2016, 24,313 patients with HIV were registered in one of the HIV treatment centres in The Netherlands

>99% of patients in the ATHENA cohort have been tested at least once for HCV
Incidence of acute HCV in HIV+ MSM in The Netherlands has increased dramatically over the past 30 years.

The Netherlands

- 1984–1999: 0.8/1000 PY\(^1\)
- 2000–2003: 9/1000 PY\(^1\)
- 2014: 11/1000 PYFU\(^2\)

In 2015\(^3\):
- 64% of newly diagnosed HCV infections were in MSM
- 28% were in heterosexual HIV+ patients
What is being done to halt the epidemic?
Dutch National Hepatitis Plan: five pillars

- Awareness and vaccination
- Identification
- Diagnosis and treatment
- Organisation of care
- Surveillance and research agenda

Broad access to DAAs in The Netherlands

- September 2014: DAAs for F3–F4 only
- November 2015: DAAs for all → unrestricted reimbursement for chronic HCV

**HIV+ MSM**
- Very eager to receive therapy
- Treatment uptake most pronounced in HIV+ MSM
HCV care in HIV+ patients in The Netherlands
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

Linked to care

Number of patients

1886

0

200

400

600

800

1000

1200

1400

1600

1800

2000

Linked to care

Currently in care and treatment ongoing or unsuccessfully or never treated

Assuming 100% SVR in patients currently on DAA therapy

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

- 41% early spontaneous clearance
- 30% died
- 6% moved abroad
- 12% lost to follow up
- 11% (n=111) HCV RNA+ never confirmed

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

<table>
<thead>
<tr>
<th>Status</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linked to care</td>
<td>1886</td>
</tr>
<tr>
<td>Retained in care</td>
<td>1454</td>
</tr>
<tr>
<td>Ever treated</td>
<td>1202</td>
</tr>
</tbody>
</table>

252 no treatment documented

Adjusted for probable spontaneous clearance (last HCV RNA test negative but to be confirmed)

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Linked to care: 1886 patients
Retained in care: 1454 patients
Ever treated: 1202 patients
Treatment completed: 1164 patients
SVR to date: 1051 patients

SVR to date:
- 1051/1454
- 72%

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

Number of patients

- Linked to care: 1886
- Retained in care: 1454
- Ever treated: 1202
- Treatment completed: 1164
- SVR: 1051
- Currently in care and treatment ongoing or unsuccessfully or never treated: 28% (403)

Assuming 100% SVR in patients currently on DAA therapy, adjusted for probable spontaneous clearance (last HCV RNA test negative but to be confirmed).
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

Graph showing the number of patients at each stage of the care cascade:
- Linked to care: 1886
- Retained in care: 1454
- Ever treated: 1202
- Treatment completed: 1164
- SVR: 1051
- Currently in care and treatment ongoing or un-successfully or never treated: 403
- Assuming 100% SVR in patients currently on DAA therapy: 322

1. Assuming SVR in n=81 on DAA

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

- Linked to care: 1886
- Retained in care: 1454
- Ever treated: 1202
- Treatment completed: 1164
- SVR: 1051
- Currently in care and treatment ongoing or unsuccessfully or never treated: 403
- Assuming 100% SVR in patients currently on DAA therapy: 322
- Adjusted for probable spontaneous clearance (last HCV RNA test negative but to be confirmed): 244

1. Assuming SVR in n=81 on DAA
2. n=78 last HCV RNA negative

Spontaneous clearance

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

Data collected in February 2017

Linked to care: 1886
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Adjusted for probable spontaneous clearance (last HCV RNA test negative but to be confirmed): 244

Worst case scenario
- 355/1454 uncured
- 24%

+111

Data collected in February 2017
HCV care cascade in HIV+ patients in The Netherlands (MSM and non-MSM)

- Linked to care: 1886
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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

Data collected in February 2017
National HIV/HCV treatment cascade in The Netherlands: 82% cured (n=1124) or on treatment (n=92)

Retained in care: 1471
Started treatment: 1284
Completed treatment: 1124
SVR: 76%

Active HCV:
- 187 (13%)
- 68 (5%)
- 92 (6%)

Treatment failure
Ongoing DAA treatment
Never treated for HCV
All

Updated 6/2017 from Boerekamps A, Newsum A et al. CROI 2017; Oral #136
HIV+ MSM with HCV
89% cured (n=844) or on treatment (n=66)

As of June 2017, updated data on HIV+ MSM with HCV in ATHENA cohort:
- 83% (844/1022) had SVR confirmed
- 6% (66/1052) were on DAA or awaiting SVR result

= 89% will be cured in the very near (3 months) future
= 111 HIV+ MSM with HCV to be treated

June 2017, all centres received a list of their population that remains to be treated with the goal of reaching 95% ASAP
Acute HCV in HIV+MSM before and after DAA roll out
Dutch Modeling study
Will treatment as prevention also work for HCV?

⇒ Immediate DAA treatment is a cost-effective HCV prevention approach that can strongly reduce, but not eliminate, the HCV epidemic among HIV-infected MSM.

Hullegie SJ et al. CROI 2016 abstract nr.536
Dutch Modeling study
Will treatment as prevention also work for HCV?

“Prediction is very difficult, especially about the future.”

Robert Storm Petersen (1882-1949)
Danish cartoonist, writer, animator, illustrator, painter and humorist
Dutch Modeling study
Will treatment as prevention also work for HCV?
Dutch Acute HCV in HIV Studies (DAHHS)

- Study hypothesis: unrestricted DAA access will result in a decrease in the number of new HCV infections in HIV+ MSM

- Goal: to evaluate the results from the modelling study with real-life data

- Methods:
  - These 17 centres treat 75% of all Dutch HIV+ MSM

Boerekamps A, et al. CROI 2017; Oral #137LB
Introduction

- DAHHS-1 study: 1 2014
- PEG-IFN + RBV + BOC for 12 weeks: GT 1 only
- 86% (49/57) cure

- DAHHS-2 study: 2 2016 and ongoing
- EBV/GRZ for 8 weeks: GT 1 or GT 4
- 67 patients included so far (from The Netherlands and Belgium)

2. ClinicalTrials.gov identifier: NCT02600325; Rijnders B, personal communication

BOC: boceprevir; EBV: elbasvir; GRZ: grazoprevir; GT: genotype; PEG-IFN: pegylated interferon; RBV: ribavirin
Results

2014

Acute HCV n=93
- GT 1 = 75 (81%)
- GT 4 = 18 (19%)

Acute HCV n=93
- 11.2 incidence/1000 PYFU (95% CI 9–14)
- 1.1% per year

17 centres provided data from both 2014 and 2016

Boerekamps A, et al. CROI 2017; Oral #137LB
Results

2014

- 11.2 incidence/1000 PYFU (95% CI 9–14)
- 1.1% per year

2016

- 5.5 incidence/1000 PYFU (95% CI 4–7)
- 0.5% per year

IRR 0.49 (95% CI 0.34–0.69)

- January–December 2014 11.2/1000
- January–June 2016 6.9/1000
- July–December 2016 4.0/1000

Boerekamps A, et al. CROI 2017; Oral #137LB

IRR: incidence rate ratio
Results

HCV RNA positive HIV+ MSM in 2014 and 2016

- 2014: 4.2%
- 2016: 1.5%

Acute HCV infections in 2014 and 2016

- 2014 (N=93)
  - GT 1: 72
  - GT 4: 18
  - GT other: 2
  - GT missing: 1

- 2016 (N=49)
  - GT 1: 27
  - GT 4: 15
  - GT other: 3
  - GT missing: 4

IRR 0.49
(95% CI 0.34–0.69)

Rijnders B, personal communication
51% decrease in acute HCV infections in 2016 compared with 2014

Observational data:
- No proof that DAA therapy uptake is the cause of the decline
- However, acute HCV was the only STI that decreased in 2016
  - Syphilis and gonorrhoea: 59 and 23% increase in 2016
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=13 HIV- patients with acute HCV in DAHHS-2 centres in 2016!
  - 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

(*) E Hoorenburg et al. AIDS 2017
Discussion

What else is needed to facilitate HCV elimination of HCV in MSM in NL?

“I know nothing about the subject, but I’m happy to give you my expert opinion.”
Discussion

Source of acute HCV now that 90% of HIV+MSM are cured?
- The remaining 10%?
- HIV- MSM with undiagnosed acute/chronic HCV?
- Acute HCV supertransmitters?
- MSM visiting the Netherlands (Amsterdam, Rotterdam)?

Very high incidence of reinfection:
- Will home based DBS HCV testing and retreat ASAP help?

Surveillance of HCV in HIV- MSM urgently needed!

Risk reduction interventions: Chemsex, slamming
What have been the success factors for The Netherlands?

- Low overall HCV prevalence, high resource setting
  => Budget impact of universal DAA “affordable” soon after EMA approval

- The HIV/HCV co-infected population is well known
  - ATHENA cohort

- Ease of initiating treatment
  - Patients (MSM in particular) have been very eager to receive therapy
  - HIV-physicians can prescribe HCV DAAs themselves (no referral necessary)
Conclusion

- For the first time in >10 years the incidence of acute HCV in HIV+ MSM in The Netherlands dropped substantially

- Unrestricted access to DAAs for the treatment of chronic (and acute) HCV is a likely explanation

- Much more is needed to come to actual elimination
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- **All patients**