4th International HIV/Viral Hepatitis Co-Infection Meeting

The Rocky Road to Viral Hepatitis Elimination:
Assuring access to antiviral therapy for ALL co-infected patients from low to high income settings

Saturday - Sunday, 22-23 July 2017
Paris, France
Meeting Summary

Dr Karine Lacombe,
INSERM UMR-S1136, IPLESP
SMIT St Antoine, AP-HP
Université Pierre et Marie Curie, Paris VI
Update on the role of community research for hepatitis prevention

- Patrizia Carrieri (from Marseillle, France) opened the meeting and welcomed you all in France

- AERLI: good example of how research can influence policies ➔ evaluation innovative harm reduction strategies (peer to peer, standardized checklist when supervising injection, tailored intervention to reduce harm

➔ health policy included in 2016 French health law, as an entry point for testing and linkage to care

**DOING WITH PEOPLE AND NOT FOR PEOPLE**
Taking stock

G. Hirnschall

NEW INFECTIONS

HEPATITIS B + C

30% REDUCTION

90% REDUCTION

10% REDUCTION

65% REDUCTION

New infections and deaths (in millions)

Years

2015 2020 2025 2030
Taking stock

G. Hirnschall

- 6 key interventions:
  - HBV Birth dose
  - PMTCT-HBV
  - safe injection practices
  - harm reduction
  - HBV treatment
  - HCV treatment
Taking stock


- HBV Birth dose
- PMTCT
- HBV Safe injection practices
- Harm reduction
- HBV Treatment
- HCV Treatment

CDC National Viral Hepatitis Surveillance System data
Taking stock

G. Hirnschall

6 key interventions:
- HBV Birth dose
- PMTCT HBV
- safe injection practices
- harm reduction
- HBV treatment
- HCV treatment

J. Brooks

Vulnerable Counties and Locations of Syringe Services Programs, USA

County-level Vulnerability to Rapid Dissemination of HIV/HCV Infection Among Persons who Inject Drugs
CDC, September 23, 2015
SSPs current as of June 2018 (Source: NASEN)
Taking stock

- In Eastern Europe, disparities in everything: quality of data, routes of transmission, HCV prevalence, access to diagnosis, access to treatment, restriction rules, etc.

- Only 4 countries have National Plans against viral hepatitis

M. Simonova
Taking stock

M. Andersson

Where are we with the priorities from Durban ?!

- HBV birth dose
- Sustainable access to antiviral TTT for monoinfected HBV
- Increased diagnostic
- Prequalified Treatment:
- End of stigmatization of PLWHCV

➤ Progress slow but on the way = paradox of the epidemic: in order to create one very contagious movement, you have to create first numerous little ones
Diagnostics

Matching the test to the setting

- Current model (Ab then RNA or Ab reflex RNA)
  - Boomer/hospital screening, OST clinics → Reliable F/U
- RDT/POCT blood (Ab)
  - Above + Screening drives, prison
- POCT saliva (Ab)
  - Screening drives, opportunistic screening (ER, prison)
- RDT (RNA)
  - Very high prevalence population – active PWID, ?OST
- DBS
  - Rural remote (no lab), hard-to-reach, time issues (ER)

J. Feld
NEW BIOMARKERS?
HBV circulating particles and secreted proteins

J. Feld
S. Fourati
SEARCH FOR A PERFECTO-CHECK!!

Diagnostics

NEW-ANTICOAGS?

HBV circulatory proteins

Blood

Hepatocyte

J. Feld

S. Fourati

N. Luhmann
Q: OK for simplification, but what if suboptimal strategy that looses patients alongside?!
Linkage to care: different strokes for different stocks?

But it is not just treatment – we need a multipronged approach

M. Hellard
Linkage to care: different strokes for different stocks?

"A nation should not be judged by how it treats its highest citizens, but its lowest ones."

Nelson Mandela

R. Altice
Linkage to care: different strokes for different stocks?
The international love life of the Swiss

Salazar-Vizcaya et al. IWHOD 2017
Linkage to care: different strokes for different stocks?

Community-based treatment model

A. Basenko

- Involvement of patients from harm reduction & OST sites and medical facilities
- Counseling before treatment
- Doctor’s examinations and consultation
- Laboratory diagnostics and examinations
- Treatment/ regimen identification
- Treatment laboratory monitoring
- Social support, re-infection prevention
- End of treatment
- Treatment results (SVR12)
Linkage to care: different strokes for different stocks?

Community-based treatment model

A. Basenko

Q: you have hundred thousand PWID and you treat only 2000... what the F. are you doing ?!!!
Treatment

Characteristics that Inform Treatment Option Selection

A. Aghemo

Treatment

Evolution of HCV therapies

- PEG-IFN + RBV + SOF
- SOF/LDV
- SOF + DCV
- OMV/PTV/RTV + DSV + RBV
- EBR/GZR
- SOF/VEL

PEG-IFN: pegylated interferon; PTV: paritaprevir; RBV: ribavirin; RTV: ritonavir; SMV: simeprevir; SOF: sofosbuvir; TVR: telaprevir; VEL: velpatasvir

Adapted from Dore G, Feld JJ. Clin Infect Dis 2015;60:1829–36
Treatment

Where would shorter durations (4-6 weeks) help?

- Prisons, particularly remand and medium security settings
- Inpatient HCV treatment (e.g. PWID with infectious complications of IDU)
- Needle Syringe Program – based treatment for PWID
- Acute HCV, including treatment of HCV reinfection
- When cost-effectiveness significantly enhanced (particularly generic LMIC settings)
Treatment

Future short duration studies

- Favourable sub-populations (F0-2, younger age, genotype/subtype): current DAA regimens
- Strategy studies: response-guided
- Acute/recent HCV
- New DAA combinations: SOF + GLE/PIB
- DAA + other classes: DAA 4 weeks + long-acting non-oral agent at week 4
Treatment

Rapid DAA scale-up is required to limit reinfection

Treatment

Strategies addressing individual-level risk: Bring a friend

Treatment Strategy Using Network-Based Approach

- “Bring your friends” strategy performed better than the random strategy
- Plausible real-world treatment strategy as most people will know their injecting partners

Treatment

• J. Rockstroh: before drinks, watch for
  – DDI: PPI!
  – HBV reactivation: HBsAg + ALT > 2N AND HBV-RNA > 2000, treat beforehand
  – Risk of HCC: occurrence ≠ recurrence (Thanks…), impacted by age, fibrosis stage, comorbidities
  – Reinfection
Clinical cases: little relaxing games just before « apéritif » time

Brain Nocardia / HBV reactivation / Vaccine escape mutant / YMDD resistance / occult HBV !

Mister PP, HCV GT3, infection reinfection relapse DDI HBc Ab !
Q: best drug for LMIC considering cost, efficacy, tolerability and access ??!!
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SOF+DCV !!!
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Difficult to say

Hum hum...
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Pfff...
What a question 😒
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DCV !! Treatment for all advocate for access!

Costs nothing! FIGHT!!
Bringing it together: the scale up

N. Martin

➢ To eliminate HCV among HIV+ PWID, need to target ALL PWID, not just HIV+
➢ Prioritization by liver disease stage likely undermining elimination efforts and may not be most cost-effective strategy
➢ Elimination likely requires aggressive HCV testing/treatment and behavior change in MSM
➢ In many LMICs, other HIV+ individuals at risk via unsafe medical/community injections, etc.: Unknown what level of intervention required for elimination among these groups, need setting-specific modeling

➢ Some reinfection is good- means you are treating people with ongoing risk!
Bringing it together: the scale up

B. Rijngers

- Treatment uptake in the Netherlands; almost no chronic HCV left for treatment among HIV+ patients (will the doctors retire?...)

- NO! thanks to acute hep C: Dutch Acute Hepatitis C Studies

- 1,1% per year in 2014, going down to 0,5% per year in 2016

- Associated with use of DAAs? Maybe, because risk behaviors could not explain the decrease (dramatic increase in other STIs)

- But thanks for the doctors, retirement is far away because reduction seems to stabilize in 2017 (why? Migration, undiagnosed HCV in HIV pos. or HIV neg. DAA not approved for acute, ongoing transmission during waiting period)
HCV – we need to treat more people

• In 2016, for every person cured of HCV, another person was newly infected

• Rates of treatment are still far too low to allow elimination of HCV worldwide by 2030

• This is despite massive sales of DAAs by pharmaceutical companies (over $61 billion between 2014-2017).

• Harm reduction needs to be intensified, to lower infection rates
Bringing it together: the scale up

A. Hill

Getting to Elimination of HCV - three main problems

1. “Diagnostic burn-out”

2. Lack of WHO pre-qualification / Regulatory “no-mans land”
   - Bioequivalence
   - Batch stability
   - Adherence to Good Manufacturing Practice

3. Voluntary licenses are too restrictive.
Elimination of Hepatitis C as a threat to public health

It has taken 15 years to get to 18 million people on ARV treatment
We have learned a lot from HIV – Hepatitis C should be easier.

We already have the drugs needed to eliminate HCV worldwide
Let’s learn from the past, and repeat this medical success story.
Bringing it together: the scale up

Central elements for HCV elimination

- Increase screening and diagnosis
- Increase uptake of effective treatment
- Expanded models of HCV management
- Political leadership
- National HCV strategies
- Policy change
Bringing it together: the scale up

P. Mélin:

“It’s just my feeling but it’s like I keep on leach two dogs on in each hand, but If I let one of the dogs go, what will happen to the other ?”

The way patients express their concern matters as much as what doctors think it is good for them: listen to them, involve them in the decisions, let the patients be at the center of the process
Research gaps in viral hepatitis

JM Pawlotski: “title = end of a field, end of my carrier...” but NO, can talk hours on the remaining gaps, we will never finish with research in hepatitis (JMP reduced his talk from 5 hours to 20mn for the sake of the moderator Jacques Normand 😊)
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- Genotype 3
- Limit for treatment before / after LT (Meld 18-20?)
- Genotypic / phenotypic resistance: fitness of viruses from failing patients (ex: R30S increases resistance)
- Natural history of HBV: treat earlier to prevent HCC even in patients with no apparent liver damage (growing evidence of liver damage in immunotolerant patients)
- Stopping NUC
- HBV cure: antivirals, immune targets...

⇒ And now, what is he gonna do now that basic research on HCV is over?!
## Broad-Spectrum Antiviral Effectiveness of SMCyplS

<table>
<thead>
<tr>
<th>Viral family</th>
<th>Virus</th>
<th>Common compound</th>
<th>Maximal fold VL reduction</th>
<th>Most potent compound</th>
<th>Maximal fold VL reduction</th>
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<td><strong>Hepatitis C virus</strong></td>
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<tr>
<td></td>
<td><strong>MERS coronavirus</strong></td>
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<td>F833</td>
<td>50% inhibition of infection*</td>
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</tbody>
</table>

(Ahmed-Belkacem et al., Nat Commun 2016;7:12777; Unpublished data)
HAV outbreak in Europe

European outbreak

- Dec. 2016: 1st RRA of ECDC reporting two GI strains among MSM in UK and Netherlands

Netherland cases: Freidl, EuroSurveill 2017
HAV outbreak in Europe

Outbreak involve most EU countries

Countries with cases infected by VRD_521_2016 (n=802)
HAV outbreak in Europe

HAV cases Jan 2016- May 2017

Sex ratio = 8
HAV outbreak in Europe

HAV cases Jan 2016- May 2017

Not only due to the past month shortage of vaccine, but also because HCP forgot to vaccinate despite the guidelines that exist for years...
Priorities for enhancing access and how to achieve them

T. Swan

Impact of DAAs and mortality in 2015

500,000 people treated with DAAs
450,000 cured (based on 90% SVR and F4 priority)

399,000 people died from HCV complications

849,000 people were cured, or died

1,300,000 more new infections than cures
Priorities for enhancing access and how to achieve them
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DNDI committed to develop specific DAA for RLS
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Stigma: please develop a druguserVIR, antistigmaVIR...
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“The law is not about justice, the law is about the law”

FixHepC buyers club
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- FixHepC buyers club
- What is a patent? How can a patent be opposed?
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- Make medicines affordable!!
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FixHepC buyers club

What is a patent? How can patent be opposed?

Welcome back at UPMC, Luis... better context though! 😊
Remerciements

• To my co-chair Marina Klein
• Jürgen Rockstroh
• Sébastien Morin
• Helena Edmonds
• Chantal Burelle
• All the co-chairs who accepted to moderate the sessions
• All the speakers for their rich, up-to-date and focused lectures
• Sponsors and donors
• And all of you who attended the workshop !

All slides and webcasts available by the end of August on the IAS website