Addressing the second 90: How can treatment scale-up across the European region be accelerated?

Jens D. Lundgren
CHIP, Rigshospitalet, University of Copenhagen
Denmark
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Prof Jens Lundgren
CHIP, Rigshospitalet, University of Copenhagen
WHO Collaborative Centre on HIV, viral hepatitis and TB
@ProfJLundgren
## Disclosure

<table>
<thead>
<tr>
<th>Relations that could be relevant for the meeting</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institution received research funding from</td>
<td>Viiv, Gilead, MSD</td>
</tr>
<tr>
<td>I do not receive personal funding from any of the companies</td>
<td></td>
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</table>

Institution also received funding from:
NIAID, European Commission, Danish National Research Foundation
HIV control

Limit transmission

Improve health for PLHIV

Diagnose and treat STD’s

Testing for HIV + linkage to care

Treatment of co-infections and co-morbidity

PEP

Promotion of safe sex behaviour

Access to ART for all PLHIV

Retention in care

PrEP

Limit transmission

Improve health for PLHIV
ART coverage and AIDS related deaths, Western and Central Europe, 2000-2016


#AIDS2018 | @AIDS_conference | www.aids2018.org
ART coverage and AIDS related deaths, Eastern Europe and Central Asia 2000-2016

HIV treatment coverage by country Eastern Europe and Central Asia, 2016

Progress toward achieving the second 90: 90% of those diagnosed on ART

Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.
Policies on ART initiation in European countries
2014 (n=49), 2016 (n=47), 2018 (n=52)

Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.

#AIDS2018 | @AIDS_conference | www.aids2018.org
What is the average length of time between a confirmed HIV diagnosis and the start of treatment?

Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.
PARTNER Study
(Partners of people on ART: a New Evaluation of the Risks)

**Design:** an observational multi-centre study of HIV serodifferent couples (MSM and HT) in which the positive partner is on ART in 75 European clinical sites:

- **Phase 1:** 2011-2014 (HT+MSM)
- **Phase 2:** 2014-2018 (MSM only)

**Primary Aim**

- To follow serodifferent partnerships that have penetrative sex without using condoms where the HIV-positive partner is on ART with a plasma HIV-1 RNA load <200 copies/mL to study risk of HIV transmission through anal sex in the absence of condom use

Rodger et al, #AIDS2018 (late breaker)
Country-specific estimates of people on ART and virologically suppressed

2004/05

<table>
<thead>
<tr>
<th>Country</th>
<th>Percentage virologically suppressed among those on ART (%)</th>
<th>Percentage on ART among those in care (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western Europe</td>
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<tr>
<td>Southern Europe</td>
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<tr>
<td>Northern Europe</td>
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<tr>
<td>East Central Europe</td>
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<tr>
<td>Eastern Europe</td>
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</tbody>
</table>

Suppressed = <500 copies/mL

Bubble size, number of people:

100 1000

EuroSIDA: Laut et al, Eurosurveillance 2018
Country-specific estimates of people on ART and virologically suppressed

<table>
<thead>
<tr>
<th>Region</th>
<th>Width</th>
<th>Height</th>
<th>Proportion virologically suppressed among those on ART (%)</th>
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</thead>
<tbody>
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<td>Western Europe</td>
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<tr>
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<tr>
<td>Eastern Europe</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Bubble size, number of people:
100, 1000

Suppressed = <500 copies/mL

EuroSIDA: Laut et al, Eurosurveillance 2018
AIM: Development of an online tool to assess % on ART and % virally suppressed (right side of CoC) on clinic/cohort level

Phase 1
- Compare existing data in EuroSIDA with surveillance data from sites in Poland, Belarus, Georgia and Serbia
- Explore sampling techniques of entire clinic population required to provide an accurate CoC

Phase 2
- Standardised tool enabling clinics to establish CoC.
- Clinics in other countries in region to validate prospectively the tool’s performance
Optimization

“making the best or most effective use of a resource”
## Major Areas for ARV Optimization in HIV Therapy

<table>
<thead>
<tr>
<th>Major Areas for ARV Optimization</th>
<th>efficacy and safety</th>
<th>simplification</th>
<th>harmonization</th>
<th>cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-formulations</td>
<td>↔</td>
<td>↑</td>
<td>↑ or ↔</td>
<td>↓</td>
</tr>
<tr>
<td>New drug class</td>
<td>↑</td>
<td>↑ or ↔</td>
<td>↑</td>
<td>↓ or ↑</td>
</tr>
<tr>
<td>Dose adjustment</td>
<td>↑ or ↔</td>
<td>↑</td>
<td>↑ or ↔</td>
<td>↓ or ↑</td>
</tr>
<tr>
<td>Drug manufacturing process</td>
<td>↔</td>
<td>↔</td>
<td>↔</td>
<td>↓</td>
</tr>
<tr>
<td>New formulations</td>
<td>↑ or ↔</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>New strategies</td>
<td>↑ or ↔</td>
<td>↑</td>
<td>↔</td>
<td>↓</td>
</tr>
</tbody>
</table>
Where Should Optimization Focus?

The money saved from switching patients off of LPV/r is enough to scale up ART to those still in need of ART.
Enthusiasm for a treatment as a function of time since first entering clinical testing

Enthusiasm

Time since initiation of phase I trials (years)
First trimester exposure and possible teratogenicity

- **Efavirenz**
  - Birth defects (efv vs no efv; n=2,026):
    - [RR] 0.78,
      - [95% CI, 0.56–1.08]
  - NTD (n=1/2,026):
    - 0.05%
      - [95% CI, < 0.01 to 0.28]

- **Dolutegravir**
  - NTD:
    - 0.9% (4 of 426) on DTG vs 0.1% (14 of 11,173) if on other ARV’s
    - Study is ongoing – 600 additional pregnancies on DTG (Feb 2019)

Response to dolutegravir/efavirenz based ART in persons on rimampinicin-based TB treatment: interim report from INSPIRING trial

<table>
<thead>
<tr>
<th>No.</th>
<th>HIV-RNA viral load / CD4 count **</th>
<th>HIV-RNA &lt; 50 copies/mL @ week 24 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>5.10 log₁₀ c/mL / 208 cells/µL</td>
<td>81% (95% CI: 72%, 90%)</td>
</tr>
<tr>
<td>44</td>
<td>5.24 log₁₀ c/mL / 202 cells/µL</td>
<td>89% (95% CI: 79%, 98%)</td>
</tr>
</tbody>
</table>

*: randomised 3:2

**: CD4 count < 50 cells/µL excluded

Dooley et al, CROI 2018
Dolutegravir (50 mg qd, day 0 - onwards) and Isoniazid and rifapentine (qw, day 4 – onwards) in 4 healthy persons: unexpected cytokine-storm related drug-induced liver injury in 2

Brooks et al, CID 2018
The case for ensuring longterm pharmacovigilance

- What we don’t know
- What we know about safety from trials

Evans and Waller, MCA 2002
Summary of optimization profiles of new ARVs recommended in 2016 WHO ARV guidelines - comparative analysis

<table>
<thead>
<tr>
<th>Optimization criteria</th>
<th>DTG</th>
<th>EFV400</th>
<th>DRV/r</th>
<th>RAL</th>
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</thead>
<tbody>
<tr>
<td><strong>Efficacy and safety</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>High virologic potency</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Low toxicity</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>High genetic barrier to resistance</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Simplification</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Available as generic FDC</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Low pill burden</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
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<tr>
<td><strong>Harmonization</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Use in pregnant women</td>
<td>?</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Use in children</td>
<td>?</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Use in HIV-associated TB</td>
<td>✓</td>
<td>?</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Few drug interactions</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low price</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
</tbody>
</table>

✓ yes  ✗ no  ? ongoing studies
Summary

- Significant progress on 2\textsuperscript{nd} 90 in last few years
  - More robust scientific evidence
    - All benefit health wise from starting early – limit active TB (incl MDR)
    - Transmission is negligible if ART is fully suppressive
  - Transformed into policy – pace varies though

- Main focus areas
  - Optimise linkage & retention in care
    - Social and medical support structures if unstable lifestyle
    - Enpower sites to construct their own “right side” of CoC
  - Continue to optimize ART
    - Continuous process
    - Use highly effective and low cost / pt ART
    - Pharmacovigilance remains paramount – interpret appropriately
  - Continue to do research – health policy driven by evidence works
How close are we to reaching the 90-90-90 targets?

Source: ECDC. Dublin Declaration monitoring 2018; validated unpublished data.
Acknowledgements

• ECDC: Teymur Noori, Anastasia Pharris, Andrew Amato, et al
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