Progress toward Universal ART Access: Innovations and Treatment 2.0

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World Health Organization
September 2013
The need for scalable, more efficient treatment models

- Simpler drugs
- Point of care diagnostics
- Community models of testing & care

CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS
From Consensus to Implementation
Treatment "2.0" Strategy: Optimizing Treatment and Promoting Efficiency Gains
Optimizing Drug Regimens
Major Strategies

- Dose reduction
- Co-formulation (FDC or co-blister pack)
- Improve API route synthesis
- Use of extended release formulations
- Substitution of drug components
- Improve drug bioavailability
- Use of new strategies (e.g.: induction-maintenance)
Perspectives on ARV drug optimization

SHORT TERM
Next 1-2 years
Improve currently available drugs and formulations
- Once daily FDC for 1st line (e.g., TDF/3TC/EFV)
- Heat stable once-daily boosted PI options for 2nd line (e.g., ATV/r, DRV/r)
- Solid pediatric formulations (sprinkles, dispersible tablets)

MEDIUM TERM
Next 2-5 years
Add new drugs/better sequencing
- Replacement of regimen components by new drugs/classes (e.g., integrase inhibitors, NRTI pro-drugs, entry blockers)

LONG TERM
Next 5-10 years
Use new strategies
- New therapeutic approaches (e.g., induction/maintenance, co-therapies, anti-latency drugs)
Looking ahead: Pipeline products summary (drug optimization)

- Improved delivery for tenofovir
  - TAF (prodrug)
  - CMX-157 (long acting)

- Potentially superior/better tolerated option to EFV in first line and/or better sequencing to 2nd line
  - DLG (once daily integrase inhibitor)
  - GSK-744 (long acting)
  - DRV/r (heat stable FDC)
Major Areas for Drug Optimization in HIV Therapy: Expected Impact

<table>
<thead>
<tr>
<th>Major Areas for Drug Optimization</th>
<th>Short Term</th>
<th>Medium Term</th>
<th>Long Term</th>
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<tbody>
<tr>
<td>Chemistry Process</td>
<td>+++</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Fixed Dose Combinations</td>
<td>++++</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Dose Reduction (prodrugs)</td>
<td>+</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>New Formulations</td>
<td>+</td>
<td>+++</td>
<td>++</td>
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<tr>
<td>New Drugs</td>
<td>+</td>
<td>++</td>
<td>++++</td>
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<tr>
<td>New Strategies</td>
<td>+</td>
<td>++</td>
<td>++++</td>
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+ = low/moderate    +++ = high    ++++ = very high
# Evolution of WHO ART guidelines

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<thead>
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<tbody>
<tr>
<td><strong>When to start</strong></td>
<td>CD4 ≤200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 200</td>
<td>CD4 ≤ 350</td>
<td>CD4 ≤ 500</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Consider 350</td>
<td>-Irrespective CD4 for TB</td>
<td>-Irrespective CD4 for TB, HBV</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- CD4 ≤ 350 for TB</td>
<td>and HBV</td>
<td></td>
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<tr>
<td>1st Line</td>
<td>8 options</td>
<td>4 options</td>
<td>8 options</td>
<td>6 options &amp; FDCs</td>
<td>2 options &amp; FDCs</td>
</tr>
<tr>
<td></td>
<td>- AZT preferred</td>
<td>- AZT preferred</td>
<td>- AZT or TDF preferred</td>
<td>- AZT or TDF preferred</td>
<td>- TDF and EFV preferred</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- d4T dose reduction</td>
<td>- d4T phase out</td>
<td>across all populations</td>
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<tr>
<td>2nd Line</td>
<td>Boosted and</td>
<td>Boosted PIs</td>
<td>Boosted PI</td>
<td>Boosted PI</td>
<td>Boosted PI</td>
</tr>
<tr>
<td></td>
<td>non-boosted</td>
<td>- IDV/r LPV/r,</td>
<td>- ATV/r, DRV/r, FPV/r</td>
<td>- Heat stable FDC: ATV/r,</td>
<td>Boosted PI</td>
</tr>
<tr>
<td></td>
<td>PIs</td>
<td>SQV/r</td>
<td>LPV/r, SQV/r</td>
<td>LPV/r</td>
<td>- Heat stable FDC: ATV/r, LPV/r</td>
</tr>
<tr>
<td>3rd Line</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>DRV/r, RAL, ETV</td>
<td>DRV/r, RAL, ETV</td>
</tr>
<tr>
<td>Viral Load Testing</td>
<td>No (Desirable)</td>
<td>No (Desirable)</td>
<td>Yes (Tertiary centers)</td>
<td>Yes (Phase in approach)</td>
<td>Yes (preferred for monitoring, use of PoC, DBS)</td>
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**Earlier initiation**

- **Simpler treatment**
- **Less toxic, more robust regimens**
- **Better monitoring**

**CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS**
From Consensus to Implementation
Expanded testing and linkage to care

WHO 2013 Recommendations:

• **Generalized epidemics**: community-based HIV testing in addition to PITC

• **Concentrated epidemics**: community-based HIV testing for key populations in addition to PITC

• Adolescent testing & counseling
New perspectives on ART monitoring

- Changing the paradigm: VL for routine monitoring, CD4 where needed
- Preparing for PoC VL: WHO to develop advice on use of different technologies at different levels of the health services
Task shifting: nurses and non-physician clinicians providing care and treatment

WHO 2013 Recommendations:

- Trained non-physician clinicians, midwives and nurses can **initiate** first-line ART and **maintain** treatment
- Trained and supervised community health workers can **dispense** ART between clinic visits.

<table>
<thead>
<tr>
<th></th>
<th>Nurse (N=404)</th>
<th>Doctor (N=408)</th>
<th>Hazard ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Cumulative failure</td>
<td>192 (48%)</td>
<td>179 (44%)</td>
<td>1.09 (0.89-1.33)</td>
</tr>
<tr>
<td>All virological failure</td>
<td>44 (11%)</td>
<td>39 (10%)</td>
<td>1.15 (0.75-1.76)</td>
</tr>
<tr>
<td>Early virological failure*</td>
<td>7 (2%)</td>
<td>6 (2%)</td>
<td>1.18 (0.49-3.51)</td>
</tr>
<tr>
<td>Late virological failure†</td>
<td>37 (9%)</td>
<td>33 (8%)</td>
<td>1.14 (0.71-1.82)</td>
</tr>
<tr>
<td>Toxicity failure</td>
<td>68 (17%)</td>
<td>66 (16%)</td>
<td>1.04 (0.74-1.45)</td>
</tr>
<tr>
<td>All lost†</td>
<td>70 (17%)</td>
<td>63 (15%)</td>
<td>1.13 (0.81-1.59)</td>
</tr>
<tr>
<td>Withdrew consent</td>
<td>18 (5%)</td>
<td>21 (5%)</td>
<td>0.87 (0.46-1.63)</td>
</tr>
<tr>
<td>Default clinic schedule</td>
<td>38 (9%)</td>
<td>32 (8%)</td>
<td>1.21 (0.76-1.93)</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>14 (4%)</td>
<td>10 (3%)</td>
<td>1.42 (0.63-3.20)</td>
</tr>
<tr>
<td>Death</td>
<td>10 (3%)</td>
<td>11 (3%)</td>
<td>0.92 (0.39-2.17)</td>
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</tbody>
</table>
Decentralization: Bringing ART closer to communities

WHO 2013 Recommendations:

• Initiation and maintenance of ART in peripheral primary facilities

• Initiation of ART in peripheral primary facilities and maintenance at community level between clinic visits.
Service integration: Responding to co-morbidities and multiple needs

WHO 2013 Recommendations:
Initiate and maintain ART in:

- TB care settings
- MCH/ANC settings
- OST settings with linkage to continued HIV care and treatment
Adherence support: combinations of interventions

WHO 2013 Recommendations:

- Minimizing out of pocket payments
- Use of fixed-dose combinations
- Strengthening drug supply system
- Patient counseling and education
- Peer support
- Nutritional support in food insecure settings
- Mobile phone text messages

Use of FDCs
Looking ahead: Potential strategies for promote long term remission/eradication (HIV Cure)
Looking ahead: Combining research agendas
Panel Discussion

Peter MacPherson
Rosanna Peeling
Roger Teck
Backup slides
New areas of WHO work 2013-2015

- HIV Self-testing – Policy Brief
- CD4 monitoring & Viral Load phase-in -- Technical document
- Early Infant Diagnosis (EID) algorithm update in light of infant ‘functional cure’
- Civil society input and demonstration projects on earlier treatment in key populations
  - IDU, MSM, SW, Adolescents, transgender individuals
Key messages from WHO self-testing meeting & policy brief (April 2013)

- Promising new approach
  - Especially for repeat testers
- Current oral fluid self-tests not give a definitive HIV result.
  - People with +ve test results must seek confirmation
- Coercive self-testing of sexual partners, family members, employees remains a human rights concern

WHO 2013 global consultation on legal, ethical, gender, human rights and public health implications of HIV self-testing, WHO, LSTM & LSHTM, April 2013, Geneva