WHO Updates from CROI 2016

Treatment and Care

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WHO HQ
Thanks for Slides:

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Silvia Bertagnolio
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CCO CROI2016 Review
Outline

• New ARV drug trials
  • INSTI, ecfTAF, LA-ARVs for treatment, monoclonal Abs

• Peadiatrics & pregnant women
  • DTG safety in pregnancy & fetus

• Earlier Treatment and Acute infection

• Cascades – how close are we to 90/90/90?

• HIV Drug resistance
  • First PrEP failure due to resistance
Benefits of INSTI

Shift To Integrase Inhibitor-based Therapy

Initial Antiretroviral Therapy

1,773 patients initiating ART between 1996 and 2014 in the UCHCC, follow-up through 2015

Regimen Type

NRTI only

Other*

NNRTI

bPI**

INSTI

bPI = LPV/r, DRV/r or ATV/r therapy

Other = includes unboosted PI and other bPI combinations

Courtesy of Thibaut Davy and Sonia Napravnik

ECHCC: UNC CFAR
HIV Clinical Cohort

Year of ART Initiation

Percentage

ECHCC: UNC CFAR
HIV Clinical Cohort

ECHCC: UNC CFAR
HIV Clinical Cohort

Eron, CROI 2016
Persistence of Initial ART

Time on Initial ART, UCHCC 1996-2014

- 1,773 patients initiating ART between
- Persistence defined as no switch in an

In CNICS cohort integrase inhibitor use was strongly associated with HIV RNA suppression
in multivariate analysis see poster 1034 Simoni et al
LATTE-2: Cabotegravir IM + Rilpivirine IM for Long-Acting Maintenance ART

- Multicenter, open-label phase IIb study
  - Primary endpoints: HIV-1 RNA < 50 c/mL by FDA snapshot, PDVF, and safety at maintenance Wk 32

**Induction Phase***

- CAB 30 mg PO QD + ABC/3TC

**Maintenance Phase**

- CAB 400 mg IM + RPV 600 mg IM Q4W (n = 115)
- CAB 600 mg IM + RPV 900 mg IM Q8W (n = 115)
- CAB 30 mg PO + ABC/3TC PO QD (n = 56)

*Pts with HIV-1 RNA < 50 c/mL from Wk 16 to Wk 20 continued to maintenance phase. 6 pts discontinued for AEs or death in induction analysis.

ART-naive HIV-infected pts with CD4+ cell count > 200 cells/mm$^3$ (N = 309)

**Latte2 Results**

**Induction period**

**Maintenance period**

Proportion of patients with virological suppression, %

<table>
<thead>
<tr>
<th>Study visit</th>
<th>BL</th>
<th>W-16</th>
<th>W-12</th>
<th>W-8</th>
<th>W-4</th>
<th>D1</th>
<th>W4</th>
<th>W8</th>
<th>W12</th>
<th>W16</th>
<th>W20</th>
<th>W24</th>
<th>W28</th>
<th>W32</th>
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<tbody>
<tr>
<td><strong>Induction</strong></td>
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<tr>
<td><strong>Maintenance</strong></td>
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**Snapshot success: D1**

- Q4W: 99%
- Q8W: 95%
- Oral CAB: 98%

Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.
# Latte2 Results

## Summary of Injection Site Reactions (ISRs)

<table>
<thead>
<tr>
<th></th>
<th>Q8W IM (n=115)</th>
<th>Q4W IM (n=115)</th>
<th>IM subtotal (N=230)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of injections</strong></td>
<td>1623</td>
<td>2663</td>
<td>4286</td>
</tr>
<tr>
<td><strong>Number of ISRs (events/injection)</strong></td>
<td>1054 (0.65)</td>
<td>1228 (0.46)</td>
<td>2282 (0.53)</td>
</tr>
<tr>
<td><strong>Grades</strong></td>
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<tr>
<td>Grade 1</td>
<td>839 (80%)</td>
<td>1021 (83%)</td>
<td>1860 (82%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>202 (19%)</td>
<td>197 (16%)</td>
<td>399 (17%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>12 (1%)</td>
<td>10 (&lt;1%)</td>
<td>22 (&lt;1%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Duration, days</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤7</td>
<td>943 (89%)</td>
<td>1121 (91%)</td>
<td>2064 (90%)</td>
</tr>
<tr>
<td>Median</td>
<td>3.0</td>
<td>3.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

- Most common ISR events overall were pain (67%), swelling (7%), and nodules (6%)
- Number of subjects reporting ISRs decreased over time, from 86% (Day 1) to 33% (Week 32)\(^a\)
- 2/230 subjects (1%) withdrew as a result of injection reactions (Q8W)

\(^a\)Represents percent of subjects with a Week 32 visit (n=220).

Margolis et al. CROI 2016; Boston, MA. Abstract 31LB.
GS-1089: Switch From Suppressive TDF-to TAF-Containing ART: Wk 48 Efficacy

- Randomized, double-blind, active-controlled phase III trial
  - Primary endpoint: HIV-1 RNA < 50 c/mL at Wk 48 by ITT
  - FDA snapshot; noninferiority margin 10%

- FTC/TAF dosing: 200/10 mg with boosted PIs; 200/25 mg with unboosted third drug.

HIV-infected pts with HIV-1 RNA < 50 c/mL, eGFR ≥ 50 mL/min while receiving FTC/TDF + third ARV (N = 663)

Switch FTC/TDF to FTC/TAF*
  - Continue third ARV (n = 333)
  - HIV-1 RNA < 50 c/mL at Wk 48, %: 94.3

Continue FTC/TDF
  - Continue third ARV (n = 330)
  - HIV-1 RNA < 50 c/mL at Wk 48, %: 93.0

Treatment difference: 1.3% (95% CI: -2.5% to 5.1%)


*FTC/TAF dosing: 200/10 mg with boosted PIs; 200/25 mg with unboosted third drug.
GS-1089: Renal Outcomes With Switch From TDF- to TAF-Containing ART

- No proximal renal tubulopathy or Fanconi syndrome in either arm

Median eGFR Change (mL/min)

<table>
<thead>
<tr>
<th>Wk</th>
<th>TAF</th>
<th>TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
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<tr>
<td>48</td>
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</tbody>
</table>

Median % Change at Wk 48

<table>
<thead>
<tr>
<th>Urine Protein-to-Creatinine Ratio</th>
<th>TAF</th>
<th>TDF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>7.7</td>
<td>14.6</td>
</tr>
<tr>
<td>Albumin</td>
<td>12.3</td>
<td>18.2</td>
</tr>
<tr>
<td>RBP</td>
<td></td>
<td>22.0</td>
</tr>
<tr>
<td>β2-M</td>
<td>-16.3</td>
<td>-39.6</td>
</tr>
</tbody>
</table>


Slide credit: clinicaloptions.com
GS-1089: BMD Changes With Switch From TDF- to TAF-Containing ART

Spine

Mean % change in BMD (95% CI)

<table>
<thead>
<tr>
<th>Wks</th>
<th>FTC/TAF, n</th>
<th>FTC/TDF, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>321</td>
<td>320</td>
</tr>
<tr>
<td>24</td>
<td>310</td>
<td>310</td>
</tr>
<tr>
<td>48</td>
<td>300</td>
<td>306</td>
</tr>
</tbody>
</table>

Hip

Mean % change in BMD (95% CI)

<table>
<thead>
<tr>
<th>Wks</th>
<th>FTC/TAF, n</th>
<th>FTC/TDF, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL</td>
<td>321</td>
<td>317</td>
</tr>
<tr>
<td>24</td>
<td>309</td>
<td>305</td>
</tr>
<tr>
<td>48</td>
<td>300</td>
<td>303</td>
</tr>
</tbody>
</table>

≥ 3% BMD Increase at Wk 48, %

<table>
<thead>
<tr>
<th></th>
<th>FTC/TAF</th>
<th>FTC/TDF</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spine</td>
<td>30</td>
<td>14</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Hip</td>
<td>17</td>
<td>9</td>
<td>.003</td>
</tr>
</tbody>
</table>

ACTG 5273: Second-line LPV/RTV + NRTIs vs LPV/RTV + RAL in African Settings

- Open-label, noninferiority phase III study
  - Primary endpoint: time to VF (confirmed HIV-1 RNA > 400 c/mL at or after 24 wks)

Wk 48: primary endpoint

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir/Ritonavir + Raltegravir</td>
<td>258</td>
</tr>
<tr>
<td>Lopinavir/Ritonavir + Best Available NRTIs*</td>
<td>254</td>
</tr>
</tbody>
</table>

HIV-infected pts with HIV-1 RNA > 1000 copies/mL after initial ART with NNRTI + NRTIs (N = 512)

*NRTIs selected according to algorithm, including substitution of zidovudine for tenofovir DF and vice versa. †Shortened to 52 wks after last enrollment.


Slide credit: clinicaloptions.com
ACTG 5273: Virologic Failure and Toxicity

- No differences in number of AIDS events, serious non-AIDS events, or deaths between arms

- Difference in VF through Wk 48:
  - RAL – NRTIs: -3.4% (95% CI: -8.4% to 2.5%)
  - Upper bound of CI < 10%: RAL noninferior
  - Upper bound of CI > 0: RAL not superior

- Cumulative probability of grade ≥ 3 toxicity event higher with LPV/RTV + NRTIs vs LPV/RTV + RAL
  - Stratified log-rank $P = .040$

- Greater increases in total, LDL-, and non-HDL cholesterol and triglycerides with RAL vs NRTIs


Slide credit: clinicaloptions.com
MK-1439-007: Doravirine + TDF/FTC vs EFV + TDF/FTC In Treatment-Naive Pts

- Doravirine: investigational NNRTI with potent activity against common NNRTI resistance mutations, QD dosing, no PPI drug–drug interactions, improved CNS safety vs EFV in early studies

- Part 2 of 2-part randomized, double-blind phase II study
  - Primary endpoint: HIV-1 RNA < 40 copies/mL at Wk 48

ART-naive HIV-infected pts with HIV-1 RNA ≥ 1000 copies/mL, CD4+ cell count ≥ 100 cells/mm³ (N = 132)*

- 42 pts receiving doravirine 100 mg QD + TDF/FTC and 43 pts receiving efavirenz 600 mg QD + TDF/FTC in part 1 of this study were included in this analysis.


*42 pts receiving doravirine 100 mg QD + TDF/FTC and 43 pts receiving efavirenz 600 mg QD + TDF/FTC in part 1 of this study were included in this analysis.

Slide credit: clinicaloptions.com
## MK-1439-007: Primary Endpoint

### Week 48 HIV-1 RNA < 40 c/mL

<table>
<thead>
<tr>
<th></th>
<th>n/N (%)</th>
</tr>
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<tbody>
<tr>
<td><strong>Doravirine</strong></td>
<td>84/108 (77.8)</td>
</tr>
<tr>
<td><strong>Efavirenz</strong></td>
<td>85/108 (78.7)</td>
</tr>
<tr>
<td><strong>Difference (95% CI)</strong></td>
<td>-1.1 (-12.2 to 10.0)</td>
</tr>
</tbody>
</table>

What’s new in TO for children and PW

• No impact of maternal TDF on infant BMD but lower WB BMC if exposed to LPV-based ART: the PROMISE trial (Siberry et al. #36)

• DTG PK: elimination half life twice as high as adults hypoglicemia and congenital abnormalities to be looked at. (Mulligan et al. #438)

• Better PK data to inform dosing of NVP for use in newborns treatment (Capparelli et al #815; Mirochnick et al #440)

• Maraviroc dosing for pediatric patients 2-<18 years old supported by safety and efficacy data which were similar to adults (Giaquinto et al. #1120)

• More evidence in support of WHO guidelines: substituting LPVr with EFV at 3 years showed lower viral rebound, higher CD4%, improved lipid profile and positively impact on bone mineral mass (Arpadi et al. #40; Munarne et al. #39)
No significant difference in Newborn mean Lumbar Spine (LS) BMC between Study Arms (pairwise comparisons)

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Est’d Mean Difference</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPVr-ZDV-3TC minus LPVr+TDF/FTC (primary)</td>
<td>-0.08 g</td>
<td>(-0.16, 0.01)</td>
<td>.09</td>
</tr>
<tr>
<td>ZDV(+sdNVP+TDF/FTCtail) minus LPV/r+TDF/FTC (secondary)</td>
<td>+0.01 g</td>
<td>(-0.08, 0.1)</td>
<td>.82</td>
</tr>
<tr>
<td>ZDV+sdNVP+TDF/FTCtail minus LPV/r+ZDV/3TC (secondary)</td>
<td>+0.09 g</td>
<td>(0, 0.17)</td>
<td>.05</td>
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</table>

No impact of maternal TDF on infant BMD but lower WB BMC if exposed to LPV-based ART: the PROMISE trial (Siberry et al. # 36)
DTG PK in Pregnant and Postpartum Women

Mulligan NA et al.  CROI 2016 Boston Abs 438

- DTG levels in pregnancy: AUC 30% lower and $C_{24}$ 40% lower in pregnancy but not significantly different than postpartum (N=4 and N=7 paired comparisons, p<0.10)
- 15/15 (100%) had RNA $\leq$50 at delivery.
- One possibly treatment-related AE: ↑ LFT
- Two SAEs: pre-eclampsia

<table>
<thead>
<tr>
<th>Median</th>
<th>2nd tri (N=9)</th>
<th>3rd tri (N=15)</th>
<th>Post (N=9)</th>
<th>Hx control</th>
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<tbody>
<tr>
<td>AUC $0-24$ (ug*hr/mL)</td>
<td>58.4</td>
<td>48.7</td>
<td>71.1</td>
<td>53.6</td>
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<tr>
<td>$C_{\text{max}}$ (ug/mL)</td>
<td>4.59</td>
<td>3.92</td>
<td>5.10</td>
<td>3.67</td>
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<tr>
<td>$C_{\text{min}}$ (ug/mL)</td>
<td>0.86</td>
<td>0.86</td>
<td>1.70</td>
<td>1.11</td>
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<tr>
<td>$T_{1/2}$ (hr)</td>
<td>10.5</td>
<td>11.2</td>
<td>12.3</td>
<td>14</td>
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</table>
Therapeutic Dosing NVP in Newborns
Capparelli E et al. CROI 2016 Boston Abs 815

- NVP 2 mg/kg QD prophylaxis dosing achieves levels >0.1 ug/mL but not therapeutic target >3 ug/mL. Newborn PK data needed.

- Evaluated PK at 1 & 2 weeks after start ART in 1st 6 infants enrolled in Botswana BPH 075 trial of early ART.
  - Median GA at birth: 37.0 ±1.9 wk
  - Median age ART start: 2.8 ±1.7 d
  - Dose NVP 6 mg/kg BID.

- Median NVP trough level: 3.6 mcg/mL (achieved target >3 ug/mL).

- No toxicity observed.
EVG/COBI/FTC/TAF in Adolescents: 48 Week Follow-Up

Gaur A et al. CROI 2016 Boston Abs 817

- TAF: enhanced intracellular but lower plasma levels TFV, thus lower toxicity.
- Phase 2/3, single-arm, open-label study of E/C/F/TAF in 50 ART-naïve adolescents.

- RNA <50 c/mL at 48 weeks: 46/50 (92)%
- Most AE Grade 1/2; no AE leading to ART d/c; no cases proximal renal tubulopathy.

Changes in Renal Biomarkers Wk 48

UPCR: urine protein:creatinine ratio; RBP: retinal binding protein; Cr: creatinine; β2M: beta-2 microglobulin

Changes in Bone Mineral Density

BMD: Bone Mineral Density; Z-Score; TBLH: Total Bone Mineral Density
P1093: Dolutegravir (DTG) in 6-12 Year Olds 48 Week Data

Wiznia A et al. CROI 2016 Boston Abs 816

- Well-tolerated, no treatment-related AE and no d/c for adverse events; good virologic/immunologic efficacy. Now studying younger age cohorts (>4 wks).

Virologic Efficacy: % VL <400

- VL <400: 78.3%
- VL <50: 74% at 48 wks (data not shown)

CD4% Changes

- Median change: +9% (7, 14)
New ARVs: Maturation inhibitors

Maturation Inhibitors (MIs): BMS-955176 Mode of Action

BMS-955176 inhibits the last protease cleavage event between capsid (CA) protein p24 and spacer peptide 1 (SP1) in Gag, resulting in the release of immature, non-infectious virions.


Eron, CROI 2016
Attachment Inhibitors

BMS-626529 Attachment Inhibitor: Proposed Mechanism of Action

No drug

Conformational changes

CD4 binding site

CD4 receptor

Cell surface

BMS-626529 binding

Conformational changes inhibited

CD4 binding Blocked

gp120

gp41

Eron, CROI 2016
Clinical Use of Antibodies

**Prevention**
- Prevent acquisition of infection
- Block transmission event

**Treatment**
- mAbs complementary to ARV drugs
- Different mechanism of action
- Potential to eliminate infected cells
- Impact the cell-associated viral reservoir

**Block viral entry**
- CD4 T-cell
- ARVs

**Cell killing**
- NK cell directed elimination of infected cells

Mascola, CROI 2016
Next Generation Treatment

- Implantable (and removable) combination antiretrovirals

- Vectored delivery of combinations of antibody-based therapy or protein-based therapy

Recombinant AAV (rAAV) features

- Transfects both dividing & non-dividing cells
- No host-genome integration & Stable Expression
- Ease to produce at high viral titer (Helper Free)
- Do not elicit significant immune response *in vivo*
- Can be used for *in vivo* gene deliveries

Eron, CROI 2016
Outline

• New ARV drug trials
  • INSTI, ecfTAF, LA-ARVs for treatment, monoclonal Abs

• Peadiatrics & pregnant women
  • DTG safety in pregnancy & fetus

• Earlier Treatment and Acute infection

• Cascades – how close are we to 90/90/90?

• HIV Drug resistance
  • First PrEP failure due to resistance
Very Early Treatment

Very Early Initiation of ART May Limit the HIV Reservoir
Decay of integrated HIV DNA during ART by Fiebig

The frequency of PBMCs harbouring integrated HIV DNA decreases rapidly upon ART initiation in FII to FIV individuals, whereas no decay is noted in subjects who started ART during chronic infection. Fiebig I remain below limit of detection.

Courtesy of Ananworanich and Chomont
RAPiT Study

Major Programmatic Outcome: ART Initiation ≤ 90 Days

- 377 ART eligible patients enrolled
- 190 standard patients
  - 54 did not initiate ≤ 90 days (28%)
  - 2 initiated ≤ 180 days
  - 52 did not initiate
  - 136 initiated ≤ 90 days (72%)
- 187 rapid patients
  - 5 did not initiate ≤ 90 days (3%)
  - 1 initiated ≤ 180 days
  - 4 did not initiate (all lost during TB workup)
  - 182 initiated ≤ 90 days (97%)

Risk difference 25% (95% CI 19 to 33%)
Crude relative risk 1.36 (95% CI 1.24 to 1.49)
RAPiT Study

Primary Protocol Outcome:
Initiated, Retained, and Suppressed ≤ 10 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Standard arm (n, %) n=190</th>
<th>Rapid arm (n, %) n=187</th>
<th>Crude risk difference [95% CI]</th>
<th>Crude relative risk* [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated ≤ 90 days</td>
<td>136 (72%)</td>
<td>182 (97%)</td>
<td>25% (19.33%)</td>
<td>1.36</td>
</tr>
<tr>
<td>Initiated ≤ 90 days and retained and suppressed by 10 months</td>
<td>96 (51%)</td>
<td>121 (64%)</td>
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</tr>
<tr>
<td>Of those not initiated ≤ 90 days and suppressed by 10 months</td>
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</tr>
<tr>
<td>Not initiated</td>
<td>54 (28%)</td>
<td>54 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated but not suppressed or with no viral load reported</td>
<td>40 (21%)</td>
<td>40 (21%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated ≤ 90 days and retained at 10 months</td>
<td>121 (64%)</td>
<td>121 (64%)</td>
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</tr>
<tr>
<td>Of those not initiated ≤ 90 days and retained at 10 months</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not initiated</td>
<td>54 (28%)</td>
<td>54 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initiated but not retained</td>
<td>15 (8%)</td>
<td>15 (8%)</td>
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</tr>
</tbody>
</table>

*Adjusting for sex and baseline CD4 count did not affect these estimates.

How Long Did It Take?

Median time in clinic between study enrollment and ARV dispensing in rapid group:
2.4 hours (IQR 2.1-2.8 hours)
Streamlined Care

1. Patient-centered approach to care
   - Welcoming environment
   - Fostering trust, connection, and a sense of investment in the patient
   - Handling adherence and retention empathetically

2. Efficient Visits for Patients and Staff
   - Rapid ART start (same day- a few days ART start )
   - Triage by nurse at all follow-up visits
   - Minimal wait time, and fast transit through clinic visit
   - Clinic visits and ART dispensation every 3 months rather than every 1-2 months

3. Viral Load Counseling
   - Structured format for discussion of undetectable and detectable results
   - Discussion tailored to patient’s ART status (pre-ART vs. early phase vs. stable ART)

4. Clinician Access
   - Telephone access for patients
   - Easy troubleshooting of questions
   - Appointment/scheduling logistics for retention

5. Appointment reminders by phone/SMS
   - One week to few days in advance
   - Retention tool

Kwarisiima, CROI 2016
Results: Retention in care (N=972)

<table>
<thead>
<tr>
<th>Week</th>
<th>350-500 CD4 cells/mm³</th>
<th>&gt;500 CD4 cells/mm³</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Week 4</td>
<td>97% 97% 97%</td>
<td>97% 97% 97%</td>
<td>97% 97% 97%</td>
</tr>
<tr>
<td>Week 12</td>
<td>97% 97% 97%</td>
<td>97% 97% 97%</td>
<td>97% 97% 97%</td>
</tr>
<tr>
<td>Week 24</td>
<td>95% 95% 95%</td>
<td>95% 95% 95%</td>
<td>95% 95% 95%</td>
</tr>
<tr>
<td>Week 36</td>
<td>92% 95% 94%</td>
<td>95% 94%</td>
<td>95% 94%</td>
</tr>
<tr>
<td>Week 48</td>
<td>91% 93% 92%</td>
<td>93% 92%</td>
<td>91% 93% 92%</td>
</tr>
</tbody>
</table>
How do Botswana’s Results Compare to UNAIDS Targets?

**UNAIDS targets:**
\[ 90\% \times 90\% \]

**Current status in Botswana:**
\[ 83\% \times 87\% \]

- Younger age was the strongest predictor of being undiagnosed, not on ART and not virologically suppressed.
- Male gender, being single or never married, and higher levels of education were also significantly associated with lower levels of coverage for the overall target.
PopART Cascade

Second 90 Target: ART uptake, among those consenting to intervention

- **Men, Zambia**: 1,413, 100% on ART
- **Men, SA**: 890, 100% on ART
- **Women, Zambia**: 8,701, 100% on ART
- **Women, SA**: 2,382, 100% on ART

Comparison:
- Pre-CHiPs: Known HIV-positive, On ART
- Post-CHiPs: Known HIV-positive, On ART

World Health Organization
Malawi Cascade

**Jan-Jun 2011**
- PLHIV: 100%
- HIV Status Known: 90%
- On ART: 81%
- Retained at 12mos: 81%
- Virally Suppressed: 73%

**Jan-Jun 2015**
- PLHIV: 100%
- HIV Status Known: 90%
- On ART: 81%
- Retained at 12mos: 81%
- Virally Suppressed: 73%
Malawian cascade

Adult (15+) ART coverage

Option B+

Projection

World Health Organization
- *In utero* infection rates ↓ from 4.2% to 1.2% in 2015; national 6 wk MTCT in 2014 estimated 1.8%, so high % MTCT may be *in utero* (or reflect move from testing high-risk to low-risk infants)

- While # birth tests ↑, tests at 7 d-2 mo ↓, with some ↑ in tests at 2-3 mo, likely reflecting transition from 6 wk to 10 wk testing; 2015 testing coverage for birth testing 79% while test coverage at 2-3 mo is only 35%.
Retention 1 Year After ART Start, Malawi
Poorest Retention in Children and Youth

Sohn A.  CROI 2016 Boston Abs 174

1-yr post-ART retention, Malawi, 2004–2014
Impact of Option B+

- N=122,582; 63% female; 13% 15-24 yrs
### Case Report: Multiclass Resistant HIV Infection Despite High Adherence to PrEP

- 43-yr-old MSM acquired multiclass resistant HIV-1 infection following 24 mos of oral once-daily TDF/FTC PrEP
- Pharmacy records, blood concentration analyses, and clinical history support recent and long-term adherence to PrEP
- PrEP failure likely result of exposure to PrEP-resistant, multiclass resistant HIV-1 strain

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Mutations Detected on Day 7 Following p24-Positive Test</th>
<th>Estimated Fold-Change in IC$_{50}$ or Change in Response (Drug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>41L, 67G, 69D, 70R, 184V, 215E</td>
<td>1.9x (ABC), 61x (3TC), 38x (FTC), 1.3x (TDF)</td>
</tr>
<tr>
<td>NNRTI</td>
<td>181C</td>
<td>43x (NVP)</td>
</tr>
<tr>
<td>PI</td>
<td>10I</td>
<td>No relevant change</td>
</tr>
<tr>
<td>INSTI</td>
<td>51Y, 92Q</td>
<td>Reduced (RAL), resistant (EVG), reduced (DTG)</td>
</tr>
</tbody>
</table>
First case HIV acquisition during PrEP due to transmitted HIVDR

Clinical Course

- Western Blot Indeterminate at 37 days; Positive at 130 days
SIDE MEETINGS
** Publication split into recent and chronically infected subjects

*Publication split into recent and chronically infected subjects
Increasing TDR in **Botswana** (Gaborone) from 2005 to 2014 in recently infected pregnant women

Botswana-Harvard AIDS Institute  
Rowley et al. 2016. *in press*
Second-line study: NNRTI/NRTI first line virologic failure – 15 countries – majority of participants from Africa or Asia

- Baseline resistance - 492 participant samples


*The TenoRes Study Group* *Lancet Infect Dis* 2016
Published Online January 28, 2015 – Abstract 503
KZN TasP Trial Cascade

The Cascade of HIV care

at a given date

Each row represents a unique individual

The Cascade of HIV care

repeated cross-sectional approach

Each row represents a unique individual

calendar time
KZN TasP Trial Cascade

Position within the cascade per exposure time

Exposure time is defined as duration since registration (or since seroconversion for individuals who seroconverted after trial registration).

- Calendar time: repeated cross-sectional approach
- Exposure time: longitudinal approach
KZN TasP Trial Cascade

Dynamic cascade per calendar time, ANRS 12249 TasP

- Infected but not diagnosed
- Diagnosed but not in care
- In care but not on ART
- On ART but not virally suppressed
- On ART & virally suppressed

Increase from ~25% to ~40% in 15 months

Position within the cascade per exposure time, ANRS 12249

Steady increase from ~20% to ~50% in 30 months