Key Messages from AIDS 2018

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- Member Governing Council LAC, IAS

IAS Educational Fund Meeting
April 3, 2019, Bogotá, Colombia.
ARV strategies

- DTG/3TC 1st line (GEMINI)
- Test and treat D/C/F/ TAF (DIAMOND)
- Switch RPV + DTG (SWORD)
- DTG Monotherapy
- DTG and Pregnancy
- DOR > DRV/r 1st line (DRIVE-FORWARD w96)
DTG Monotherapy studies

- 2 small RCT: DTG monotherapy vs continuation of triple therapy
  
  - **EARLY SIMPLIFIED TRIAL** (Zurich, monocentric): 99 patients with documented primary infection and with cART initiation within 180 days after estimated day of infection + suppressed viremia for at least 48 weeks

  **Results**: DTG monotherapy non-inferior compared to cART (98.5% vs 100%) at W48.

Braun DL, IAC 2018, Abs. TUAC0102
DTG Monotherapy studies

- 2 small RCT: DTG monotherapy vs continuation of triple therapy
  - **MONCAY** (France, multicentric): 158 patients with HIV RNA < 50 c/mL > 12 months, on DTG/ABC/3TC

  **Results**: DTG monotherapy non-inferior at W24 (94% vs 96%), however by W48: 7 virologic failures on DTG monotherapy with resistance emergence to INSTI in 2/7 vs 0 VF on DTG/ABC/3TC. DSMB recommended to stop immediately the study.

**Conclusion**: DTG monotherapy should not be offered as an option for maintenance in suppressed patients

Hocqueloux L, IAC 2018, TUAB0103
GEMINI-1 and -2 Phase III Study Design

Identically designed, randomized, double-blind, parallel-group, multicenter, noninferiority studies

- ART-naive adults
- VL 1000-500,000 c/mL
- No evidence of pre-existing viral resistance
- No HBV infection or need for HCV therapy

<table>
<thead>
<tr>
<th>Double-blind phase</th>
<th>Open-label phase</th>
<th>Continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG + 3TC (N=716)</td>
<td>DTG + TDF/FTC (N=717)</td>
<td>DTG + 3TC</td>
</tr>
</tbody>
</table>

Baseline stratification factors:
- HIV-1 RNA (vs >100,000 c/mL)
- CD4 (≤200 vs >200 cells/mm³).

Primary endpoint
HIV-1 RNA <50 c/mL (ITT-E snapshot)

-10% noninferiority margin for individual studies.

Cahn et al. AIDS 2018, TUAB0106LB.
GEMINI
Pooled Snapshot Outcomes at W48: ITT-E and Per Protocol Populations

Virologic outcome

Adjusted treatment difference (95% CI)a

DTG + 3TC is non-inferior to DTG + TDF/FTC
GEMINI 1 and 2

Confirmed Virologic Withdrawals Through W48: ITT-E Population

<table>
<thead>
<tr>
<th>Variable, n (%)</th>
<th>DTG + 3TC (N=716)</th>
<th>DTG + TDF/FTC (N=717)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVW</td>
<td>6 (&lt;1)</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>Treatment-emergent resistance</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Overall safety and tolerability at W48: comparable between the 2 regimens
- Fewer drug-related AEs with DTG + 3TC
- Change in renal and bone biomarkers significantly favors DTG + 3TC

- 2% of participants in each arm had baseline HIV-1 RNA >500,000 c/mL

Cahn et al. AIDS 2018, TUAB0106LB.
Initial ARV Therapy

- **1981**: Initial report of AIDS cases
- **1983**: HIV-1 isolation
- **1985**: HIV-1 isolation
- **1987**: NRTIs
  - AZIDOTIMIDINA (AZT) Monotherapy
  - Increased survival
  - Short-time efficacy (1-2 years)
  - Poor tolerability
  - Significant adverse effects

Increased survival
Short-time efficacy (1-2 years)
Significant adverse effects
Survival
Failure in 2-3 years
DIAMOND : D/C/F/TAF for Test and Treat strategy

- N = 109 (2% female, 32% black, 23% VL > 5 log, 21% CD4 < 200)
- Median time from HIV diagnosis to screening/baseline : 5 days (0 to 14)
- Only 29% were enrolled within 48 hours after HIV diagnosis
- At W24
  - Continuing study : 91%, discontinued for safety reasons : 1%
  - HIV RNA < 50 c/ml : 81%, < 200 c/ml : 87%

Huhn GD, IAC 2018, Abs. WEPEC200
ARV Surveillance During Pregnancy

- Limited data available on safety of ART during pregnancy and lactation
  - Approximately 5-yr mean lag between ARV approval and availability of data in pregnancy, with no pregnancy data available for 3/7 ARVs approved since 2010

- Current data on newer ARVs (ie, INSTIs, ETR, TAF) insufficient to exclude even a 2-fold increase in overall birth defects or rare events such as neural tube defects

- Risk of serious birth defects associated with any drug exposure at conception greater than for exposure during pregnancy, although clinical trials may not distinguish between the two
  - Neural tube defects likely to occur before Day 28 post conception
July 15, 2018: Updated prevalence of DTG exposure at conception is 4/596 (0.67%, 95% CI 0.26%, 1.7%).

-- 95% CI still does not overlap with any other exposure group.

May 1, 2018

<table>
<thead>
<tr>
<th>NTDs/Exposures</th>
<th>DTG-Conception</th>
<th>Any Non-DTG ART-Conception</th>
<th>EFV-Conception</th>
<th>DTG Started During Pregnancy</th>
<th>HIV-NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/426</td>
<td>14/11,300</td>
<td>3/5,787</td>
<td>0/2.812</td>
<td>61/66,057</td>
<td></td>
</tr>
<tr>
<td>% with NTD (95% CI)</td>
<td>0.94% (0.37%, 2.4%)</td>
<td>0.12% (0.07%, 0.21%)</td>
<td>0.05% (0.02%, 0.15%)</td>
<td>0.00% (0.00%, 0.13%)</td>
<td>0.09% (0.07%, 0.12%)</td>
</tr>
<tr>
<td>Prevalence Difference (95% CI)</td>
<td>ref</td>
<td>-0.82% (-0.24%, -2.3%)</td>
<td>-0.89% (-0.31%, -2.3%)</td>
<td>-0.94% (-0.35%, -2.4%)</td>
<td>-0.85% (-0.27%, -2.3%)</td>
</tr>
</tbody>
</table>
Tsepamo Updated Analysis Plan

• Next formal analysis will occur after 31 March 2019
  – Will include women already exposed to DTG from conception prior to recent guideline change
  – Plans in place to expand from 8 to 18 sites, increasing from 45% to 72% of births in the country

• Final analysis in 2019 to include:
  – NTDs
  – All major malformations
  – Other adverse birth outcomes (stillbirth, preterm)
## WHO 2018 recommendations for first-line ART

<table>
<thead>
<tr>
<th>Population</th>
<th>Preferred</th>
<th>Alternatives</th>
<th>Special situations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult men and adolescent boys</td>
<td></td>
<td>TLD&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Pregnant (from eight weeks after conception) and breastfeeding women and adolescent girls</td>
<td>TLD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>TLE600</td>
<td>AZT+3TC+ EFV600&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TLE400</td>
<td>TDF+3TC (or FTC)+PI/r&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Women and adolescent girls with effective contraception or not of childbearing potential</td>
<td>TLE600</td>
<td>TLE400</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF+3TC (or FTC)+PI/r&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Women and adolescent girls of childbearing potential who want to become pregnant and have no effective contraception</td>
<td>TLE600</td>
<td>TLE400</td>
<td>AZT+3TC+ EFV600&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF+3TC (or FTC)+PI/r&lt;sup&gt;c&lt;/sup&gt;</td>
<td>TDF+3TC (or FTC)+ RAL</td>
</tr>
</tbody>
</table>

<sup>a</sup> In PLHIV with TB using rifampicin, the dose of DTG needs to be increased to 50 mg twice daily.
<sup>b</sup> NVP may be used in special circumstances where alternative options are not available.
<sup>c</sup> If national prevalence of EFV pretreatment drug resistance exceeds 10% or if no other alternatives are available.

\[
TLD = TDF + 3TC + DTG \\
TLE = TDF + 3TC (or FTC) + EFV
\]

→ A woman-centered approach: promoting human rights + promoting gender equality – enable women to make informed choices
Important Considerations for Improving Contraceptive Options

• 60% of HIV positive women of child bearing age are <26 yo
• 50% of HIV positive women who became pregnant did not desire pregnancy
• 80-90% of women use condoms as their primary contraceptive method.
• Complications secondary to abortion are now the number one cause of maternal mortality in Botswana.
• Concepts of “Family Planning” do not necessarily translate culturally. It is much better to speak of contraception.
• Reproductive choice and safe guarding HIV positive women pregnancy outcomes - across all ART regimens – is the goal.
TB coinfection

- Preventive therapy
- MDR-TB recommendations
- DTG and Tuberculosis (INSPIRING)
# Tuberculosis Preventive Therapy in PEPFAR Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>TB Preventive Therapy Completion, % (numerator/denominator)</th>
<th>Number of PLHIV on ART</th>
<th>Proportion of PLHIV on ART that initiated TPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Democratic Republic of the Congo</td>
<td>53% (10466/19845)</td>
<td>57704</td>
<td>34%</td>
</tr>
<tr>
<td>Haiti</td>
<td>67% (5082/7562)</td>
<td>85195</td>
<td>9%</td>
</tr>
<tr>
<td>Kenya</td>
<td>85% (165914/195319)</td>
<td>1011712</td>
<td>19%</td>
</tr>
<tr>
<td>Lesotho</td>
<td>28% (2324/8368)</td>
<td>140658</td>
<td>6%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>49% (62503/128223)</td>
<td>909929</td>
<td>14%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>71% (43193/61161)</td>
<td>720272</td>
<td>8%</td>
</tr>
<tr>
<td>Swaziland</td>
<td>85% (13976/16381)</td>
<td>145891</td>
<td>11%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>61% (2186/3590)</td>
<td>60113</td>
<td>6%</td>
</tr>
</tbody>
</table>

[Table 1. TB Preventive Therapy in Selected PEPFAR Countries]

**Figure 1.** Numbers of patients who initiated B preventive therapy, with completion rates, by age, gender and country.

**Abstract 11669**
Rapid Communication:

Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB)

Table 1. Grouping of medicines recommended for use in longer MDR-TB regimens

<table>
<thead>
<tr>
<th>GROUP</th>
<th>MEDICINE</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A:</strong></td>
<td>Levofloxacin <strong>OR</strong></td>
<td>Lfx</td>
</tr>
<tr>
<td>Include all three medicines</td>
<td>Moxifloxacin</td>
<td>Mfx</td>
</tr>
<tr>
<td>(unless they cannot be used)</td>
<td>Bedaquiline(^1,4)</td>
<td>Bdq</td>
</tr>
<tr>
<td>Linezolid(^2)</td>
<td></td>
<td>Lzd</td>
</tr>
<tr>
<td>Clofazimine</td>
<td></td>
<td>Cfz</td>
</tr>
<tr>
<td>Cycloserine <strong>OR</strong></td>
<td></td>
<td>Cs</td>
</tr>
<tr>
<td>Terizidone</td>
<td></td>
<td>Trd</td>
</tr>
<tr>
<td><strong>Group B:</strong></td>
<td>Ethambutol</td>
<td>E</td>
</tr>
<tr>
<td>Add both medicines</td>
<td>Delamanid(^3,4)</td>
<td>Dlm</td>
</tr>
<tr>
<td>(unless they cannot be used)</td>
<td>Pyrazinamide(^5)</td>
<td>Z</td>
</tr>
<tr>
<td></td>
<td>Imipenem-cilastatin <strong>OR</strong></td>
<td>Ipm-Cln</td>
</tr>
<tr>
<td></td>
<td>Meropenem(^6)</td>
<td>Mpm</td>
</tr>
<tr>
<td></td>
<td>Amikacin <strong>(OR Streptomycin)</strong>(^7)</td>
<td>Am</td>
</tr>
<tr>
<td></td>
<td>Ethionamide <strong>OR</strong></td>
<td>Eto</td>
</tr>
<tr>
<td></td>
<td>Prothionamide</td>
<td>Pto</td>
</tr>
<tr>
<td></td>
<td><em>p</em>-aminosalicylic acid</td>
<td>PAS</td>
</tr>
</tbody>
</table>
Drug susceptibility testing and mortality in patients treated for tuberculosis in high-burden countries

Kathrin Zürcher, Marie Ballif, Lukas Fenner, Sonia Borrell, Peter M. Keller, Joachim Gnokoro, Olivier Marcy, Marcel Yotebieng, Lameck Diero, E. Jane Carter, Neesha Rockwood, Robert J. Wilkinson, Helen Cox, Nicholas Ezati, Alash’le G. Abimiku, Jimena Collantes, Anchalee Avihingsanon, Kamon Kawkitinarong, Miriam Reinhard, Rico Hömke, Robin Huebner, Sebastien Gagneux, Erik C. Böttger, Matthias Egger, on behalf of the International Epidemiology Databases to Evaluate AIDS (IeDEA)

22nd International AIDS Conference (AIDS 2018), 23-27 July 2018, Amsterdam Netherlands
### Concordance and discordance of DST results

<table>
<thead>
<tr>
<th>Concordance / discordance of DST results</th>
<th>Reference laboratory</th>
<th>Local laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordance</td>
<td>513 (80.9%)</td>
<td></td>
</tr>
<tr>
<td>Pan-susceptible</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mono-resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-XDR and XDR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discordance potentially leading to under treatment</td>
<td>23 (3.6%)</td>
<td></td>
</tr>
<tr>
<td>MDR</td>
<td></td>
<td>Pan-susceptible</td>
</tr>
<tr>
<td>Pre-XDR and XDR</td>
<td></td>
<td>MDR</td>
</tr>
<tr>
<td>Discordance potentially leading to over treatment</td>
<td>67 (10.6%)</td>
<td></td>
</tr>
<tr>
<td>Pan-susceptible</td>
<td></td>
<td>Mono-resistance</td>
</tr>
<tr>
<td>Pan-susceptible</td>
<td></td>
<td>MDR</td>
</tr>
<tr>
<td>Mono-resistance</td>
<td></td>
<td>Pre-XDR or XDR</td>
</tr>
<tr>
<td>MDR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other discordance</td>
<td>31 (4.9%)</td>
<td></td>
</tr>
<tr>
<td>Pan-susceptible</td>
<td></td>
<td>EMB, SM</td>
</tr>
<tr>
<td>Mono-resistance</td>
<td></td>
<td>Pan-susceptible</td>
</tr>
<tr>
<td>INH, MOX</td>
<td></td>
<td>MDR</td>
</tr>
<tr>
<td>IHN, PZA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment was adequate in 96.8% of patients with concordant DST results compared to 77.7% with discordant results.
Results

Mortality during TB treatment by concordance / discordance of DST

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>No. of deaths (%)</th>
<th>aOR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concordance</td>
<td>466</td>
<td>46 (9.9)</td>
<td>1</td>
</tr>
<tr>
<td>Discordance potentially leading to under treatment</td>
<td>22</td>
<td>9 (40.9)</td>
<td>9.53 (1.04-87.32)</td>
</tr>
<tr>
<td>Discordance potentially leading to over treatment</td>
<td>61</td>
<td>6 (9.8)</td>
<td>1.01 (0.26-3.88)</td>
</tr>
<tr>
<td>Other discordance</td>
<td>24</td>
<td>6 (25.0)</td>
<td>4.40 (2.14-9.03)</td>
</tr>
</tbody>
</table>

*adjusted for sex, age, sputum microscopy, and HIV status.
## Results

Mortality during TB treatment by degree of drug resistance

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>No. of deaths (%)</th>
<th>aOR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan-susceptible</td>
<td>359</td>
<td>23 (6.4)</td>
<td>1</td>
</tr>
<tr>
<td>Mono-resistance</td>
<td>39</td>
<td>10 (25.6)</td>
<td>5.38 (2.62-11.04)</td>
</tr>
<tr>
<td>MDR</td>
<td>146</td>
<td>24 (16.4)</td>
<td>3.43 (1.91-6.16)</td>
</tr>
<tr>
<td>Pre-XDR/XDR</td>
<td>29</td>
<td>10 (34.5)</td>
<td>11.33 (2.41-53.3)</td>
</tr>
</tbody>
</table>

*adjusted for sex, age, sputum microscopy, and HIV status.
**Results**

**Mortality during TB treatment by treatment adequacy**

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>No. of deaths (%)</th>
<th>aOR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan-susceptible, adequate treatment</td>
<td>336</td>
<td>20 (6.0)</td>
</tr>
<tr>
<td>Pan-susceptible, inadequate treatment</td>
<td>23</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td>Any resistance, adequate treatment</td>
<td>199</td>
<td>36 (18.1)</td>
</tr>
<tr>
<td>Any resistance, inadequate treatment</td>
<td>15</td>
<td>8 (53.3)</td>
</tr>
</tbody>
</table>

* adjusted for sex, age, sputum microscopy, and HIV status.
INSPIRING: SAFETY AND EFFICACY OF DOLUTEGRAVIR-BASED ART IN TB/HIV CO-INFECTED ADULTS AT WEEK 48


1Johns Hopkins University School of Medicine, Baltimore, MD, USA; 2Desmond Tutu HIV Foundation, Cape Town, South Africa; 3Clinical HIV Research Unit, Johannesburg, South Africa; 4Instituto de Pesquisa Clínica Evandro Chagas FIOCRUZ, Rio de Janeiro, Brazil; 5Hospital Dos de Mayo, Lima, Peru; 6Fiocruz/Tropical Medicine Foundation Dr Heitor, Vieira Dourado, Manaus, Brazil; 7Fundación Huesped, Buenos Aires, Argentina; 8Regional Center For Prevention and Treatment of AIDS and Infectious Diseases, Russia; 9ViiV Healthcare, Brentford, UK; 10GlaxoSmithKline, Stockley Park, UK; 11ViiV Healthcare, Melbourne, Australia; 12GlaxoSmithKline, Upper Merion, PA, USA; 13ViiV Healthcare, Research Triangle Park, NC, USA
INSPIRING: Phase IIIb Study Design

Phase IIIb, randomized, multicenter, open-label, non-comparative, active-controlled, parallel-group study

TB therapy

HIV/TB co-infected ART-naive adults

HRZE (2 months)  HR (4 months)\(^a\)

DTG (50 mg BID) + 2 NRTIs (n=69)  DTG (50 mg QD) + 2 NRTIs

EFV (600 mg QD) + 2 NRTIs (n=44)

Screening −28 to −14 days  Day 1  24 weeks  52 weeks  Continuation Phase (ART)

Interim analysis: % <50 copies/mL (modified Snapshot)

End of randomized phase

Primary endpoint at Week 48: % <50 copies/mL (modified Snapshot)

Inclusion criteria

- HIV-1 RNA ≥1000 copies/mL and CD4+ ≥50 cells/mm\(^3\)
- Pulmonary, pleural, or lymph node tuberculosis with RIF-sensitive MTB confirmed by culture or GeneXpert
- RIF-containing TB treatment started up to a maximum of 8 weeks before randomization and no later than the screening date

DTG:EFV 3:2 randomization stratified by

- Screening plasma HIV-1 RNA ≤100,000 or >100,000 copies/mL
- Screening CD4+ ≤100 or >100 cells/mm\(^3\)

\(^a\)Duration of continuation phase of TB treatment according to local guidelines (up to 7 months in some countries).

ClinicalTrials.gov, NCT02178592.

Dooley et al. 22nd International AIDS Conference; Amsterdam, the Netherlands. Slides TUAB0206.
Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DTG (n=69)</th>
<th>EFV (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median (range), years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50 years, n (%)</td>
<td>33 (18-62)</td>
<td>32 (20-50)</td>
</tr>
<tr>
<td></td>
<td>9 (13)</td>
<td>2 (5)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>30 (43)</td>
<td>16 (36)</td>
</tr>
<tr>
<td><strong>African heritage/African, n (%)</strong></td>
<td>47 (68)</td>
<td>29 (66)</td>
</tr>
<tr>
<td><strong>HIV-1 RNA, median (Q1, Q3), log_{10} copies/mL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100,000 copies/mL, n (%)</td>
<td>5.10 (4.74, 5.47)</td>
<td>5.24 (4.50, 5.67)</td>
</tr>
<tr>
<td></td>
<td>44 (64)</td>
<td>24 (55)</td>
</tr>
<tr>
<td><strong>CD4+ cell count, median (Q1, Q3), cells/mm³</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤100 cells/mm³, n (%)</td>
<td>208 (128, 410)</td>
<td>202 (92, 354)</td>
</tr>
<tr>
<td></td>
<td>13 (19)</td>
<td>12 (27)</td>
</tr>
<tr>
<td><strong>Current TB conditions, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td>65 (94)</td>
<td>44 (100)</td>
</tr>
<tr>
<td>Lymph node TB</td>
<td>5 (7)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Pleural TB</td>
<td>5 (7)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Time from start of TB therapy to Day 1, median (Q1, Q3), days</strong></td>
<td>35.0 (28.0, 44.0)</td>
<td>33.5 (26.0, 50.5)</td>
</tr>
<tr>
<td><strong>Most common NRTI backbone, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>46 (67)</td>
<td>31 (70)</td>
</tr>
<tr>
<td>TDF/3TC</td>
<td>4 (6)</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>

*Participants could have had pulmonary TB with pleural or lymph node TB.*
Virologic and Immunologic Results in the ITT-E Population in Randomized Phase

 Modified FDA Snapshot Analysis (ITT-E)
 Proportion of participants with HIV-1 RNA <50 copies/mL (95% CI)

- DTG (n=69)
- EFV (n=44)

INSPRING pharmacokinetic data

<table>
<thead>
<tr>
<th>Time</th>
<th>n</th>
<th>DTG $C_T$ (ng/mL) geometric mean (%CVb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 8</td>
<td>42</td>
<td>870 (118)</td>
</tr>
<tr>
<td>Week 24</td>
<td>23</td>
<td>964 (263)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>n</th>
<th>DTG $C_T$ (ng/mL) geometric mean (%CVb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 36</td>
<td>27</td>
<td>854 (208)</td>
</tr>
<tr>
<td>Week 48</td>
<td>26</td>
<td>881 (281)</td>
</tr>
</tbody>
</table>

DTG $C_{\text{tau}}$, when administered twice daily with RIF, was similar to DTG 50 mg once daily without RIF and to previously reported data for DTG 50 mg once daily in phase II/III HIV trials.

- Median change from baseline in CD4+ cell count (Q1, Q3) at Week 48
  - DTG, 220 cells/mm$^3$ (111, 271)
  - EFV, 190 cells/mm$^3$ (104, 252)

*aModified FDA snapshot: NRTI switch for tolerability not counted as failure.*

Dooley et al. 22nd International AIDS Conference; Amsterdam, the Netherlands. Slides TUAB0206.
# Treatment outcome. TB- and Non–TB-Associated IIRIS

<table>
<thead>
<tr>
<th>Treatment Success</th>
<th>DTG (n=69)</th>
<th>EFV (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Success</td>
<td>61 (88)</td>
<td>40 (91)</td>
</tr>
<tr>
<td>Treatment failure</td>
<td>0</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Died</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Not evaluated / Lost to follow-up</td>
<td>8 (12)</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants with events sent to adjudication committee for TB-associated IIRIS</th>
<th>DTG (n=69)</th>
<th>EFV (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met criteria for TB-associated IIRIS</td>
<td>4 (6)(^a)</td>
<td>4 (9)(^b)</td>
</tr>
<tr>
<td>Possibly met criteria for TB-associated IIRIS</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Participants with events sent to adjudication committee for non–TB-associated IIRIS</th>
<th>DTG (n=69)</th>
<th>EFV (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met criteria for non–TB-associated IIRIS</td>
<td>1 (1)(^c)</td>
<td>0</td>
</tr>
<tr>
<td>Possibly met criteria for non–TB-associated IIRIS</td>
<td>1 (1)(^d)</td>
<td>0</td>
</tr>
</tbody>
</table>

No participant in either arm permanently discontinued treatment because of IIRIS

\(^a\)1 × Grade 1, 2 × Grade 2, and 1 × Grade 3. \(^b\)3 × Grade 2 and 1 × Grade 4.

\(^c\)Grade 2 (IRIS and strongyloidiasis; also experienced TB-associated IIRIS). \(^d\)Grade 1 (herpes zoster).

Dooley et al. 22nd International AIDS Conference; Amsterdam, the Netherlands. Slides TUAB0206.
Emergent Issues in TB

- Preventive therapy is useful but with a limited coverage
- Treatment of MDR/RR-TB include new drugs, combinations and treatment duration
  - Cost and availability
  - Adequate treatment needs DST
- DTG at double dose (bid) is virologically non-inferior to EFV during TB-treatment
  - Cost and availability
- Implementation of a human rights-based approach to TB.
Retention in care

PARTNER 2

Universal Treatment & test and treat

Retention in pregnant women
90:90:90 Cascade – Europe 2016

PLWHIV diagnosed
- WEST: 86%
- CENTRE: 83%
- EAST: 76%

Diagnosed on ARV
- WEST: 90%
- CENTRE: 73%
- EAST: 46%

On ARV with undetectable VL
- WEST: 92%
- CENTRE: 78%
- EAST: 74%

PLWHIV with undetectable VL
- WEST: 72%
- CENTRE: 45%
- EAST: 26%

Source: ECDC. Dublin Declaration monitoring 2018

Teymur N, IAC 2018, Abs. MOAS3502
Health status among LTFU: Kenya, Tanzania, Uganda

Random sample of adults on ART who were LTFU

- Alive, in care
- Alive, no care
- Dead

Top reasons for LTFU

- Transportation (33%)
- Work or child care (24%)
- Felt healthy (22%)
- Transportation (57%)
- Near work/home (27%)
- Family obligations (21%)

PARTNER2: HIV Risk in Serodiscordant MSM Partners

- Multicenter, observational, prospective study of HIV serodiscordant couples in which the HIV-positive partners received suppressive ART
  - PARTNER1: 2010-2014 (MSM and heterosexuals)
  - PARTNER2: 2014-2018 (MSM only)

- Primary aim: estimate within-couple HIV transmission risk for serodiscordant MSM having condomless sex while HIV-positive partner had HIV-1 RNA < 200 copies/mL
  - No PEP or PrEP use reported by HIV-negative partner
  - Linked infections established by phylogenetic analysis of HIV-1 pol and env sequences isolated from plasma or PBMCs

783 MSM couples contributed 1596 CYFU

PARTNER2: HIV Transmission

No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 c/mL

Unlinked transmissions occurred in 15 initially HIV-negative MSM partners

PARTNER2: HIV Transmission

No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 c/mL.

Unlinked transmissions occurred in 15 initially HIV-negative MSM partners.

3 large community-based randomised trials investigating the impact of multi-faceted, enhanced HIV treatment and prevention strategies (complex intervention package)

- **BCPP/Ya Tsie**: community-randomized trial (Botswana): patient-centered package of interventions (that also included on other diseases such as hypertension) including community-based HIV testing, linkage-to-care, and expanded ART criteria (with universal ART from June 2016).
  - The intervention resulted in a 31% reduction in community HIV incidence.
  - Will the full package now roll-out?
3 large community-based randomised trials investigating the impact of multi-faceted, enhanced HIV treatment and prevention strategies (complex intervention package)

- **SEARCH trial** (East Africa-Uganda/Kenya): HIV “test and treat” strategy with universal ART, randomizing 32 communities.
  - The intervention did not result in reduced HIV incidence,
  - but significant increases in ART initiation and virologic suppression
  - and reductions in HIV-mortality (21% reduction) and HIV-TB incidence (59% reduction).
3 large community-based randomised trials investigating the impact of multi-faceted, enhanced HIV treatment and prevention strategies (complex intervention package)

- **MaxART**, stepped-wedge randomized-controlled health systems trial (Swaziland): intervention offering ART regardless of CD4 count + clinical mentoring and community mobilization support. 3405 patients were enrolled across 14 clinics (40% during the intervention).
  - 86% retention was observed under the intervention (universal test and treat) compared with 80% under standard of care at 12 months, a significant difference
Effect of PrEP Uptake on HIV Diagnoses: United States

- Comparison of HIV diagnoses in people 13 yrs of age or older* vs PrEP uptake rates† from 2012 to 2016

For 38 jurisdictions with available viral suppression data, significant association between PrEP uptake and decrease in HIV diagnoses persisted after controlling for state viral suppression level.

†CDC method estimated PrEP indications; national database covering > 83% of prescriptions supplied via commercial pharmacies and validated algorithm excluding non-PrEP FTC/TDF quantified unique persons using PrEP.
ANRS Prevenir: Daily vs On-Demand TDF/FTC Oral PrEP

- Multicenter, open-label, prospective cohort study in Paris

**Beginning of Study**
- May 3, 2017

**Current Analysis**
- July 2, 2018

**End of Study**
- May 31, 2020

HIV-negative adults at high risk of HIV infection with inconsistent condom use; CrCl ≥ 50 mL/min; HBsAg negative in on-demand arm (N = 1594)*

**Daily TDF/FTC PrEP †**
- (n = 724)

**On-Demand TDF/FTC PrEP †**
- (2-1-1: 2 doses before sex, 1 dose QD for 2 days after sex) (n = 870)

*Participants enrolled in arm of their choice with ability to switch
†Plus condoms, gels, risk reduction and adherence counseling, questionnaire on sexual behavior. Follow-up every 3 mos with STI and/or HIV testing, plasma creatinine measurement.

- Predominantly MSM (98.8%), white (85.2%); median age: 36 yrs
- Primary endpoint: ≥ 15% reduction in new HIV diagnoses among MSM in Paris vs rate reported by National Surveillance network in 2016
- Secondary endpoints: PrEP adherence, sexual behavior, safety

ANRS Prevenir: HIV Incidence

<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>HIV incidence/100 PY (95% CI)</td>
<td>0 (0-0.8)</td>
<td>0 (0-0.7)</td>
</tr>
</tbody>
</table>

- Mean follow-up: 7 mos
- Overall HIV infections averted, n = 85
  - Assuming incidence of 9.17/100 PY as reported for IPERGAY study in Paris
- High incidence of STI and new HCV infection (1.2/100 pt-year)
- Overall incidence of study discontinuation: 3.3/100 PY, including PrEP discontinuations of 1.5/100 PY
  - No participant discontinued PrEP due to drug-related adverse events.
- Study planned to enroll 3,000 participants and F-U of 3 years
  - Objective: reduction of HIV incidence of 15% in Paris

*On-demand PrEP strategy not FDA approved.
OLE: PrEP Reduces Incidence of HIV Even With Incomplete Adherence

- Open-label extension of ATN 082, iPrEx, and US Safety Study PrEP trials in HIV-negative MSM and transgender women (N = 1603; 76% receiving daily oral TDF/FTC)\[1\]

### HIV Incidence and Drug Concentrations

<table>
<thead>
<tr>
<th>TFV-DP in fmol/punch</th>
<th>&lt; 2 Tablets/Wk</th>
<th>2-3 Tablets/Wk</th>
<th>4-6 Tablets/Wk</th>
<th>7 Tablets/Wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLOQ</td>
<td>0</td>
<td>350</td>
<td>700</td>
<td>1000</td>
</tr>
<tr>
<td>HIV Incidence per 100 Person-Yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>1</td>
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<tr>
<td>2</td>
<td>1</td>
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<tr>
<td>4</td>
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</tr>
<tr>
<td>5</td>
<td></td>
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</tr>
</tbody>
</table>

### Follow-up, %\[2\]

- Off PrEP: 26
- On PrEP: 12

### Risk reduction, %\[2\]

- Off PrEP: 44
- On PrEP: 84

### 95% CI\[2\]

- Off PrEP: -31 to 77
- On PrEP: 21 to 99

**Risk reduction, 95% CI (combined):**

- 86 to 100

---

## Oral PrEP: Recommended Dosing

<table>
<thead>
<tr>
<th>CDC(^1)</th>
<th>FDA(^2)</th>
<th>IAS-USA(^3)</th>
</tr>
</thead>
</table>
| - Recommended for daily use only  
  - Not recommended as coitally timed or other noncontinuous use | FTC/TDF indicated for PrEP once daily | - Recommended for daily use  
  - Optional recommendation for on-demand use only for MSM with infrequent sex |

- **On-demand use: 2-1-1 dosing**  
  - Double dose before sex,  
  - 1 dose 24 hrs after first dose,  
  - 1 dose 48 hrs after first dose

---

Integrating oral HIV pre-exposure prophylaxis (PrEP) in a public family planning facility and youth center to inform national roll out in Zimbabwe

22nd International AIDS Conference
24 July 2018

Presented by Makaita Gombe, Clinton Health Access Initiative (CHAI)

Co-authors: Y. Mangwendeza, G. Ncube, N. Zwangobani, B. Cakouros, A. Svisva, A. Mangwiro, M. Murwira, A. Mkwamba, A. Erlwanger, M.L. Prust

The authors have no conflicts of interest to declare.
## Healthcare worker training and preparation

### ART Training

- 2-week ART training (because sites were not providing ART)

### PrEP Training

- One day PrEP training on screening, initiation, and adherence counselling

### PrEP M&E Training

- Focused on completion of PrEP client form and PrEP register

## Client outreach and enrollment

- Increasing client awareness
  - Group education in waiting rooms
  - Integration with family planning, VMMC and other services

- Screening and enrollment
  - HIV testing
  - HIV risk assessment integrated into counselling *(see below)*
  - PrEP offered and clients given 1 month supply, followed by 3 months

## MOHCC HIV risk assessment for PrEP screening

In the past 6 months:
- How many people did you have vaginal or anal sex with?
- Did you use a condom every time you had sex?
- Did you have a sexually transmitted infection?

**Do you have a sexual partner who has HIV?** □ Yes □ No □ DK*
- If 'yes' has your partner been on ART for more than 6 months?
- If 'yes' is your partner virally suppressed?
• Uptake differed significantly between the rural and urban facilities: 9% uptake in the rural Chimanimani site compared to 2.7% in the urban Harare site.

• Majority of clients initiated on PrEP did not know their partner’s status or were in a new or known sero-discordant partnership.
Emerging issues in PrEP

• Risk compensation and higher STI rates,
• Elevated risk of new HVC infections among MSM
• Vulnerabilities of marginalised populations (overcome stigma and inequality toward MSM, TG women, homeless, PWID, adolescents and younger age (25-29), migrants and indigenous populations).
• Prevention programmes: importance of comprehensive sexuality education + address the psychosocial conditions
• Risk perception may be low. Offer PrEP through health system friendliness
• Are there certain patients in whom you would recommend on-demand PrEP
• What are your PrEP recommendations for women and for adolescents
• What is the ideal place to offer PREP
• Cost for the health system

We are still short of the UNAIDS goals of linking
3 million persons to PrEP by 2020
SAVE THE DATE

10TH IAS CONFERENCE ON HIV SCIENCE (IAS 2019)

MEXICO CITY, MEXICO | 21-24 JULY 2019

Muchas Gracias