IAS 2022 Conference Highlights

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No conflicts of interest or relationships to disclose
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IAS 2022 Updates

• Prevention
  - HPTN 083 and 084 updates
  - PrEP Inequity

• Treatment
  - ALLIANCE: TAF v TDF for HIV/HBV co-infection
  - ADVANCE updates
  - CAB/RPV delivery
HPTN 083: demonstrated superiority of CAB-LA as compared to oral TDF/FTC for HIV prevention in **MSM and TGW who have sex with men**

- 12.5% (570) of participants enrolled were TGW (self identified)
- ~58% reported gender affirming hormone therapy (GAHT) use
- HIV incidence during blinded phase was 1.8% (TDF/FTC) versus 0.54% (CAB-LA), HR 0.34
  - Similar incident STI rates
- No meaningful difference in AEs
Transgender Women (TGW) in HPTN 083: GAHT with CAB-LA

Grinsztejn et al. IAS 2022
• CAB-LA safe and effective for TGW

• Consistent with overall HPTN 083 findings, TGW on CAB-LA had lower incidence of HIV as compared to TDF/FTC

• GAHT does not appear to impact CAB concentrations
HPTN 084: Previously demonstrated superiority of CAB-LA as compared to daily oral TDF/FTC for HIV prevention in **individuals assigned female at birth**

- HIV incidence: CAB 0.20 v TDF/FTC 1.85 (per 100 person years), HR 0.12
- Update 12 months post unblinding
Updated Efficacy and Safety Results from HPTN 084

Delany-Moretiwe et al. IAS 2022
Updated Efficacy and Safety Results from HPTN 084

Cumulative Pregnancy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Total n=132</th>
<th>CAB n=63</th>
<th>TDF/FTC n=69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>57</td>
<td>23</td>
<td>34</td>
</tr>
<tr>
<td>Known pregnancy outcomes*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births</td>
<td>61</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>Pregnancy loss</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=37 weeks</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20-36 weeks</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&lt;20 weeks**</td>
<td>13</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Includes multiple births
**Includes ectopic pregnancy, elective and spontaneous abortion
• Continued CAB superiority over oral TDF/FTC in HIV prevention in those female at birth

• Three additional CAB group infections (all with either no or poor use)

• Need more evaluation of CAB in pregnancy in open-label extension
Trends in PrEP inequity by race and census region, United States 2012-2021

The PrEP-to-Need Ratio (PnR) is the number of PrEP users divided by the number of new diagnoses in a given year. PnR serves as a measurement of how PrEP use compares to the PrEP in a population.
Treatment
ALLIANCE: Phase 3 RCT of BIC/TAF/FTC versus TDF/FTC + DTG as Initial Treatment in HIV/HBV Co-Infected adults (Wk 48 results)

- HIV/HBV coinfected: maintain TFV based regimen (with 3TC or FTC)
- No randomized studies of TDF v TAF based ART in coinfection initiating treatment

Randomization stratified by:
- HBeAg (positive vs negative)
- HBV DNA (< vs ≥8 log10 IU/mL)
- CD4+ cell count (< vs ≥50 cells/μL)

HIV-1 RNA <50 copies/mL (FDA Snapshot algorithm), 12% noninferiority margin
HBV DNA <29 IU/mL (missing = failure analysis), 12% noninferiority margin
ALLIANCE: Phase 3 RCT of BIC/TAF/FTC versus TDF/FTC + DTG as Initial Treatment in HIV/HBV Co-Infected adults (Wk 48 results)

<table>
<thead>
<tr>
<th></th>
<th>B/F/TAF n=121</th>
<th>DTG + F/TDF n=122</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (IQR)</td>
<td>31 (27, 39)</td>
<td>32 (25, 38)</td>
</tr>
<tr>
<td>Female at birth, n (%)</td>
<td>9 (7)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>108 (89)</td>
<td>106 (87)</td>
</tr>
<tr>
<td>White</td>
<td>10 (8)</td>
<td>9 (7)</td>
</tr>
<tr>
<td>Black</td>
<td>2 (2)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Median body mass index, kg/m² (IQR)</td>
<td>22.2 (19.9, 24.7)</td>
<td>21.7 (19.3, 23.7)</td>
</tr>
<tr>
<td>Median HIV-1 RNA, log₁₀ copies/mL (IQR)</td>
<td>4.7 (4.2, 5.1)</td>
<td>4.7 (4.3, 5.0)</td>
</tr>
<tr>
<td>HIV-1 RNA &gt;100,000 copies/mL, n (%)</td>
<td>38 (31)</td>
<td>34 (28)</td>
</tr>
<tr>
<td>Median CD4 cells/µL (IQR)</td>
<td>245 (127, 383)</td>
<td>236 (121, 380)</td>
</tr>
<tr>
<td>CD4 count &lt;200 cells/µL, n (%)</td>
<td>46 (38)</td>
<td>52 (43)</td>
</tr>
<tr>
<td>Median HBV DNA, log₁₀ IU/mL (IQR)</td>
<td>8.0 (6.5, 8.4)</td>
<td>8.1 (6.6, 8.5)</td>
</tr>
<tr>
<td>HBV DNA ≥8 log₁₀ IU/mL, n (%)</td>
<td>60 (50)</td>
<td>66 (54)</td>
</tr>
<tr>
<td>HBeAg positive, n (%)</td>
<td>92 (76)</td>
<td>97 (80)</td>
</tr>
<tr>
<td>ALT &gt;ULN, n (%)*</td>
<td>60 (50)</td>
<td>47 (39)</td>
</tr>
</tbody>
</table>
ALLIANCE: Phase 3 RCT of BIC/TAF/FTC versus TDF/FTC + DTG as Initial Treatment in HIV/HBV Co-Infected adults (Wk 48 results)

- HIV endpoint: B/F/TAF non-inferior
- HBV endpoint: TAF superior

- Mean CD4 change from baseline, cells/µL (95% CI): B/F/TAF +200 (175, 226), DTG + F/TDF +175 (152, 198)
ALLIANCE: Phase 3 RCT of BIC/TAF/FTC versus TDF/FTC + DTG as Initial Treatment in HIV/HBV Co-Infected adults (Wk 48 results)

- TAF: Non-significant higher rates of HBsAg loss and seroconversion
- TAF: Higher rates of eAg loss (not significant) and seroconversion (significant)
ALLIANCE: Phase 3 RCT of BIC/TAF/FTC versus TDF/FTC + DTG as Initial Treatment in HIV/HBV Co-Infected adults (Wk 48 results)

- As compared to DTG + F/TDF, B/F/TAF:
  - Noninferior at achieving HIV-1 RNA suppression
  - Superior at achieving HBV DNA suppression
  - Higher rates of HBeAg seroconversion
  - With similar safety

...is TAF better?
ADVANCE: TFV/FTC + DTG v TDF/FTC/EFV, 192 week

- ADVANCE prior demonstrated non inferiority of TFV (TDF or TAF)/FTC + DTG versus TDF/FTC/EFV
  - Weight gain in DTG arms, TAF + DTG >> TDF + DTG
  - Weight gain most pronounced in women, lower CD4 counts, and higher VL
• Body weight increases:
  - +8.9 kg (TAF/FTC + DTG)
  - +5.8 kg (TDF/FTC + DTG)
  - +3.3 kg (TDF/FTC/EFV)

• Risk of clinical obesity highest in TAF/FTC + DTG (29% by week 192), female patients, and those with higher baseline BMI

• Proportion of women developing clinical obesity by week 192:
  - 43% (TAF/FTC + DTG)
  - 27% (TDF/FTC + DTG)
  - 20% (TDF/FTC/EFV)

Venter et al. NEJM 2019; Venter et al. IAS 2022
ADVANCE: Treatment emergent metabolic syndrome

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>TAF/FTC+DTG</th>
<th>TDF/FTC+DTG</th>
<th>TDF/FTC/EFV</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>50/335 (15%)</td>
<td>32/330 (10%)</td>
<td>23/337 (7%)</td>
</tr>
<tr>
<td>Women</td>
<td>40/199 (20%)</td>
<td>23/169 (12%)</td>
<td>29/191 (10%)</td>
</tr>
<tr>
<td>Men</td>
<td>10/136 (7%)</td>
<td>9/141 (6%)</td>
<td>4/145 (3%)</td>
</tr>
</tbody>
</table>

Risk is significantly higher for TAF/FTC+DTG (p<0.05) for all patients, and for women.
• Substantial weight gain differences maintained at 192 week follow up
  - Most pronounced in TAF + DTG, women, those with higher baseline BMI
• Higher risk of metabolic syndrome and clinical obesity in TAF/FTC + DTG
• TAF v TDF: No significant differences in HIV RNA suppression or renal/bone AEs
  - Both with continued higher rates of VL suppression compared to TDF/FTC/EFV
CAB/RPV Administration

• Thigh\(^1\), Subcutaneous and IM\(^2\) delivery?
  - PK parameters and safety/tolerability of CAB/RPV IM in thigh acceptable
  - High concentration CAB/RPV safe, tolerable at various injection sites

• Delivery in PWH with and without detectable viremia
  - 51 patients initiating IM CAB/RPV → 39 with at least 2 follow up injections
    - 24 suppressed, 15 viremic
  - 100% of those suppressed maintained VS after initiating injections
  - 80% (12) viremic achieved and maintained VS
  - remaining three had 2 log decline by median of 22 days\(^3,4\)

\(^1\)Han et al, IAS 2022; \(^2\)Benn et al, IAS 2022, \(^3\)Christopoulos et al, IAS 2022, \(^4\)Christopoulos et al CID 2022
Takeaways

• CAB-LA continues to be:
  - a superior and safe PrEP option for people assigned female at birth, including in pregnancy
  - safe and effective for TGW, including those on GAHT
  - Improving with respect to delivery methods

• Continued (and worsening) inequities in access to and use of PrEP in the US persist regionally and by race/ethnicity

• TAF >> TDF in HIV/HBV coinfection (maybe?)

• DTG (especially with TAF) continues to be associated with weight gain, risk of metabolic syndrome, and clinical obesity
Acknowledgment

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