Disclosures

Grant funding from Vir Biotechnology, Inc as a clinical trial investigator.
Data presented in this presentation offer a limited glimpse of health inequities that exist within a larger social context. Racism, not race, creates and perpetuates health disparities.

The MWAETC, in alignment with the American Medical Association, encourages characterizing race as a social construct, rather than an inherent biological trait, and supports ending the practice of using race as a proxy for biology in medical education, research and clinical practice.

January 2022
Outline

• Highlight abstracts and symposium presentations from CROI focusing on:
  • Tuberculosis
  • COVID-19
  • Hepatitis C

• One abstract in detail per topic

• “Lightning round” with brief summaries
Tuberculosis
Dolutegravir PK with daily 1HP for TB preventive therapy

• ACTG A5372 trial of pharmacokinetics of DTG in PWH receiving 1HP for LTBI
• 1HP noninferior to 9H for TB prevention (BRIEF-TB); all PWH on EFV ART
• RPT metabolism can decrease DTG levels
• DOLPHIN study of 3HP (weekly) with DTG (50mg daily) found no decrease in VL suppression, GM DTG trough 546ng/ml
• No data on effect on DTG levels/VL suppression of 1HP given with DTG
• Key implications for treatment-shortening of LTBI rx for PWH worldwide
Dolutegravir PK with daily 1HP for TB preventive therapy

ACTG 5372 Study Design

- Meets all criteria for enrollment
- Entry (Day 0) Intensive PK Sampling
- Complete Study Supplied 4 weeks of once daily RPT 600mg + INH 300mg (1HP) + DTG 50mg twice daily + Once daily dual Nucleoside Therapy + Non-study supplied Pyridoxine (25 or 50mg once daily)
- End of 1HP (Day 28) Intensive PK Sampling
- Interim Analysis Presented here (n=25 of 36 accrual target)
- Review of Arm 1 DTG BID + 1HP PK data and Simulation of DTG QD + 1HP PK Data

If supported by initial data & modeling, Arm 2 will open, to evaluate DTG QD PK with 1HP

- Adults w HIV, VL <20
- LFTs <2.5x ULN
- No TAF (RPT interaction)
- Not BF/pregnant
- N=25 enrolled
Dolutegravir PK with daily 1HP for TB preventive therapy

- Used minimum DTG threshold: 158 ng/ml, 5th percentile DTG trough from a 10mg/day sampling study

- 24/25 had HIV RNA levels <50 copies/mL at d28.

- One ppt had HIV VL of 160 copies/mL at day 28 (DTG conc 2162 ng/mL), repeat VL of <50 copies/mL on day 42.
Dolutegravir PK with daily 1HP for TB preventive therapy

- DTG trough concentrations with BID DTG and 1HP were higher than standard daily DTG
- Decrease in DTG trough concentrations d3-d28 → dose dependent induction of DTG metabolism
- All DTG trough above DTG target
- No hypersensitivity or serious AEs
- PK, VL suppression, safety data → bid DTG dosing with 1HP
- Next will investigate daily DTG with 1HP (Stage 2 of study)
TB Lightning Round

• Cross GB et al. OA-76: Rosuvastatin may have benefit as host-directed adjunctive therapy for TB based on in vitro data. RCT (N=137) of TB treatment SOC vs. TB treatment + rosuvastatin 10mg daily x 8 weeks for Rif-S TB. Outcome: Time to culture conversion. Result: No difference in time to culture conversion (42 d in both arms, p=0.188). [few HIV+ included]

• Kakande E. et al OA-75: Implementation science study – education & support for mid-level clinic managers resulted in modest increase in TB preventive therapy (IPT) initiations for PLWH in Uganda, after a nationwide “IPT push.”

• Nuermberger E. Symposium: New TB drugs and drug classes in pipeline, long-acting formulations of TB drugs in development.

• Dorman S. Symposium: Progress with treatment-shortening regimens for TB treatment (4M for adults and children) and prevention (3HP, 1HP).
COVID-19
Adverse Birth Outcomes: COVID-19 & HIV

- Higher rates of adverse parental & birth outcomes in people with COVID-19 seen globally
- PLWH have worse outcomes from COVID-19
- Little evidence on interaction/combination.
- 13 sites from Tsepamo study in Botswana, birth outcomes Sept 2020 – Nov 2021
  - Women with known HIV status
  - COVID screening test within (-14d, +3d) delivery

Flow diagram of women with COVID by HIV status

- 20,410 deliveries during study period
- 11,483 (56%) screened for COVID
- 539 (4.7%) COVID+
- 144 (5.6%) HIV+ COVID+
- 392 (4.3%) HIV- COVID+

Women living with HIV were more likely to test COVID+ at delivery (p<0.01)
Adverse Birth Outcomes: COVID-19 & HIV

Maternal deaths were high with COVID, particularly during Delta, but not worse with HIV

<table>
<thead>
<tr>
<th>Maternal Deaths</th>
<th>COVID Status</th>
<th>Age Adjusted Risk Ratios (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>COVID+</td>
<td>19 (4%)</td>
</tr>
<tr>
<td></td>
<td>COVID-</td>
<td>12 (0.1%)</td>
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<tr>
<td></td>
<td></td>
<td>31.6 (15.4, 64.7)</td>
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<tr>
<td>HIV Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV+</td>
<td></td>
<td>4 (3%)</td>
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<tr>
<td></td>
<td></td>
<td>3 (0.1%)</td>
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<tr>
<td></td>
<td></td>
<td>23.3 (5.3,102.8)</td>
</tr>
<tr>
<td>HIV-</td>
<td></td>
<td>15 (4%)</td>
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<tr>
<td></td>
<td></td>
<td>9 (0.1%)</td>
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<tr>
<td></td>
<td></td>
<td>35.6 (15.7,81.0)</td>
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<tr>
<td>Variant</td>
<td></td>
<td></td>
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<tr>
<td>Pre-Delta</td>
<td></td>
<td>3 (2%)</td>
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<tr>
<td></td>
<td></td>
<td>5 (0.1%)</td>
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<tr>
<td></td>
<td></td>
<td>13.9 (3.4, 57.2)</td>
</tr>
<tr>
<td>Delta</td>
<td></td>
<td>15 (5%)</td>
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<tr>
<td></td>
<td></td>
<td>5 (0.1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>56.3 (20.5, 154.7)</td>
</tr>
</tbody>
</table>

**ART use very high:** 97% of women on ARVs, >75% started ART prior to conception

*Maternal COVID-19 vaccination status not available
*<15% fully vaccinated in Botswana by late 2021
Adverse Birth Outcomes: COVID-19 & HIV

- 5.5% absolute risk of stillbirth in infants born to mothers with COVID-19
COVID-19 + HIV Lightning Round

• Moller et al, poster 760: Sweden national registry of all people hospitalized with COVID-19 Feb 1, 2020 – August 31, 2021. N=121 PWH (93% VLUD; med CD4=560), 64764 PWoH hospitalized. Severe COVID-19 = ICU or 90d mortality. No increased odds of severe COVID-19 outcomes in PWH vs. PWoH (aOR=0.88, ns/CI incl 1)

• Ballivian et al, poster 642: Argentinian cohort of N=844 PWH with COVID-19. 85% on ART, 68% VLUD. 20% hospitalization.

• Spinelli et al poster 888: Viral suppression increased during COVID in SF Ward 86 cohort of PWH (N=1816) w/ increased social services, outreach, housing, and return to in-person visits
Hep C Re-infection

- Decrease in HCV incidence shortly following unrestricted access to DAAs, strongest effect seen in people/MSM with HIV in clinical care
- Reinfection rates still too high to reach HCV elimination goals
- COVID-19 impact on testing, treatment initiation, harm reduction services
- Early re-treatment with DAAs recommended for re-infection

Risk factors for HCV reinfection

Mucosal HCV transmission among MSM
- Receptive condomless anal intercourse
- Number of casual sex partners
- Fisting
- Sharing sex toys
- Sharing anal douching equipment
- Sharing equipment during nasally administered drug use
- Engaging in anal intercourse causing rectal trauma with bleeding
- Ulcerative STI

Percutaneous HCV transmission among PWID
- Sharing equipment for injecting drug use
- Recent IDU

Maria Prins, Case-based Liver Workshop
Hep C Lightning Round

• Requena et al, Poster 532: In French cohort of PWH w/ VL suppression, higher risk of death (all-cause mortality) in first 36 months of SVR in HIV+/HCV+ pts cured with DAAs vs HIV+/HCV- pts (matched on f/u time, age, gender, BMI, CD4 nadir, transmission RF) despite HCV cure.

• Ma et al, Poster 537: Among PWH in CNICS cohort, transgender women more likely to have HCV than cis men and women, more likely HCV viremic than CM, but once in care received DAAs as readily as cis PWH.
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