Learning Objectives

After attending this presentation, learners will be able to:

▪ Describe new research data related to treatment and prevention of TB in people living with HIV
▪ Describe the implications of new research related to opportunistic infections and other infectious disease complications in people living with HIV

What's New in TB Treatment and Prevention
Safety and PK of Weekly Rifapentine/Isoniazid (3HP) in Adults with HIV Receiving Dolutegravir

- N=61; (1 pt had elevated Cr prior to HP)
  - 60 pts completed all 12 doses
  - 1 pregnancy at week 24
  - VL WNL at all time points
  - CRP WNL at all time points
  - VL < 40 copies/ml at BL, wk 9 during DTG + 3HP in all pts
    - 1 pt with VL 2,300 copies/ml wk 24 → resuppressed after adherence counseling
  - 3 pts had grade 2 or 3 AE
    - 1 pt with flu-like illness

Dooley K, et al., CROI 2019; Abstr. 80L

TSHEPISO Cohort: Women with HIV, No TB Disease, IPT Exposed and Unexposed During Pregnancy

- IPT use during pregnancy was not associated with a higher rate of poor maternal or infant outcomes (N=152)

Dooley KA, et al. CROI 2019; Abstr. 77

Early Bactericidal Activity (EBA) of High-Dose INH in MDR-TB

- High dose INH is a component of short course therapy of MDR-TB
- 2 key INH resistance mutations
  - katG → high-level resistance
  - inhA → low-level resistance
- AS312 evaluated EBA (as measured by serial sputum culture colony counts [cfu] and time to positivity [TTP] in liquid culture) of different doses of INH in pts with MDR-TB

Dooley KA, et al. CROI 2019; Abstr. 82
Early Bactericidal Activity (EBA) of High-Dose INH in MDR-TB

- 58/59 randomized pts (98%) completed treatment
- 9 pts had grade 3 AEs unrelated to INH
- There were no grade 4 SAEs or deaths

Dooley KA, et al. CROI 2019; Abstr. 62

Double Dose Darunavir/Ritonavir + Rifampin for TB Treatment

- Rationale
  - Rifabutin expensive and not widely available
  - LPV/RTV double dose + rifampin effective but not well tolerated
  - Darunavir/RTV better tolerated than LPV/RTV
- Comparison of DRV/RTV 800 mg/100 mg BID or 1600 mg/200 mg once daily + DTG 50 mg BID + rifampin 450mg or 600 mg

Maartens G, et al. CROI 2019; Abstr. 81

Double Dose Darunavir/Ritonavir + Rifampin for TB Treatment

- Double dose DRV/RTV + rifampin has unacceptable hepatotoxicity risk in PLWH without TB
- Rifampin co-administration markedly reduced DRV concentrations
- Twice daily, but not once daily DRV/RTV may achieve adequate DRV trough concentrations

Maartens G, et al. CROI 2019; Abstr. 81
DELIBERATE: QTc Effects of Bedaquiline, Delamanid or Both in MDR-TB

- Both drugs prolong QTc interval
  - Peak effect at 16-18 weeks for BDQ and 8 weeks for DLM
- RCT comparing BDQ, DLM or both in 84 pts with MDR-TB
  - Median age 35; 25% women; 37% HIV

Maartens G, et al. CROI 2019; Abstr. 84

Other Opportunistic Infections

CMV Viremia and Mortality in Patients with Cryptococcal Meningitis

*Samples were selected randomly and the consent forms were approved by the institutional review board
*All patients were tested for CMV on admission and additional testing was done as needed

Figure 3: Kaplan-Meier Survival Curve by CMV status

- Mortality: 3% (1/33) vs 4% (22/555) 
- Log Rank P value: 0.08
Cryptococcal Antigenemia in Pts with Virologic Failure on ART

- Retrospective review and CrAg testing on stored samples from 1,186 pts with VF and HIV RNA ≥ 1000 copies/ml
  - 35 pts CrAg positive
  - 2 pts developed CM, successfully treated
- 6-month meningitis-free survival (N=25) was 56% in those who received some fluconazole
  - 42% without fluconazole
- CrAg screening should be considered in persons with VF; could be limited to those with VL > 5,000 copies/ml

Primary PJP Prophylaxis in Virally Suppressed PLWH

- 9,743 pts with 18,550 person/ys of followup eligible for 3 simulated trials:
  - Trial A = Continuation of PJP prophylaxis vs. stopping
  - Trial B = Starting PJP prophylaxis vs. no prophylaxis
  - Trial C = On PJP prophylaxis vs. off PJP prophylaxis

- HR estimates for occurrence of PJP for:
  - Trial A = HR 2.0 (0.61, 6.4); P = 0.3
  - Trial B = HR 2.8 (0.8, 9.9); P = 0.1
  - Trial C = HR 1.2 (0.5, 3.2); P = 0.8

- Conclusion:
  - Overall low incidence of PJP
  - In virally suppressed pts, irrespective of CD4 cell count, the risk of PJP is low and similar for pts on and off prophylaxis
HPV Vaccine Plus LEEP for Recurrent Cervical HSIL in Women with HIV Infection

- Randomized, double-blind placebo controlled trial in 180 women with HIV and cervical HSIL
- HPV vaccine (VLP types 6, 11, 16, 18) or saline placebo at entry, week 4 and week 26
- All women had LEEP at week 4 followed by colposcopic biopsy, cervical cytology at week 16, 52
- 97% completed vaccine and had biopsy result at week 26 or 52 – 53% had LEEP margins (+) for HSIL

Firnhaber C, et al. CROI 2019; Abstr. 14

Sofosbuvir/Ledipasvir HCV Treatment in HCV/HIV-Coinfected Pregnant Women

- 170 HCV+ pregnant women
- 29 pts screened to enroll 9 pts who completed study medication and delivered 9 infants
  - 100% SVR in 8 pts, 1 still in followup
  - 5 infants completed 12 months F/U; 4 still ongoing

Chappell CA, et al. CROI 2019; Abstr. 87

Pregnancy and Delivery Outcomes Following Maternal HCV Treatment

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N (%) or Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Related Adverse Events</td>
<td>5 (56%)</td>
</tr>
<tr>
<td>Maternal Related Adverse Events Grade ≥2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Vaginal Delivery</td>
<td>5 (56%)</td>
</tr>
<tr>
<td>Gestational age at delivery (weeks + days)</td>
<td>39+2 (36+6, 41+0)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3,290 (2,600, 4,160)</td>
</tr>
<tr>
<td>Infant Length of Hospital Stay (days)</td>
<td>3 (2, 12)</td>
</tr>
<tr>
<td>Infant Related Adverse Events</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Infant HCV RNA at Last Visit (copies/mL)</td>
<td>0 (0, 0)</td>
</tr>
</tbody>
</table>

Chappell CA, et al. CROI 2019; Abstr. 87
HCV Reinfection Among MSM with HIV Infection in NY

- NY Acute Hepatitis C Surveillance
- Network longitudinal study
  - HCV clearance by either SVR 12 after treatment or spontaneous clearance with undetectable VL for >12 weeks post infection
  - Acute reinfection → 1st noted ALT elevation or HCV viremia
- 304 cleared HCV
  - 33 reinfected and cleared → incidence rate 4.4/100 PY (primary rate 1.4/100 PY)
  - 6 second reinfections → incidence rate 8.7/100 PYs

Fierer DA, et al. CROI 2019; Abstr. 86

Functional “Cure” of HBV in Persons with HIV/HBV Co-Infection

- Retrospective study of 501 pts
  - 98% on active HBV ART→ 10% HbsAg clearance over ~11 years
  - AIDS diagnosis, lower baseline CD4, Hispanic, HbeAg (−) associated with higher seroconversion rate
- Prospective cohort of 256 pts ART-naive, median BL CD4 202 cells/mm³
  - All started on TDF-based ART→ 10% HbsAg clearance over 2 years
  - Lower BL CD4, female sex, lower BL HBV DNA associated with higher seroconversion rate
- Retrospective cohort of 359 pts median BL CD4 359 cells/mm³
  - Started on a TDF- or TAF-based ART regimen → 18.4% HbsAg seroconversion over median of 41 months
  - AIDS diagnosis, lower CD4 gain on ART, no TDF in regimen associated with lower seroconversion rate

Jain MK, et al. CROI 2019; Abstr. 624; Chihota BV, et al., CROI 2019; Abstr. 625; Boesecke C, et al., CROI 2019; Abstr. 627

Summary

- Globally, tuberculosis is the most common cause of death in PLWH; research is intensifying and the field is changing rapidly
  - Research in TB in resource-limited settings will have a substantial impact on our ability to treat and prevent TB in high-resource settings
- As ART regimens (and access to them) continue to improve, other OIs continue to decline in incidence and impact
  - Those with virologic failure, if not recognized and treated, will continue to be at risk for OIs
  - Key to success inOI treatment and prevention → effective ART
Question-and-Answer