IAS 2021 Conference Highlights

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Grant funding: Vir Biotechnology, Inc.
• Long-acting ART
• Capella study (26-wk) results, lenacapavir for highly treatment-experienced PWH, (Molina et al, A-LB-IAS2021-02605)
• Calibrate study (28-wk): LEN for treatment initiation (Gupta et al, OALB03-02211)

• Long-acting PrEP
• Safety & PK of monthly islatravir – week 24 (A-LB-IAS2021-02361, Hillier et al)

• Co-infection (TB, Cryptococcus) treatment lighting round
Lenacapavir (LEN): first-in-class HIV capsid inhibitor; *in vitro* data for effect against NRTI, NNRTI, INSTI–resistant HIV → use for highly treatment-experienced (HTE) PWH
Capella Study: LEN for HTE PWH

FDA-snapshot week 26 efficacy data (N=36)

- Good safety & tolerability
  - no SAEs related to drug or AEs leading to discontinuation
  - median CD4 increase 81 over 26 weeks, none <50 at 26wk

Molina et al, A-LB-IAS2021-02605
**Calibrate Study, Gupta et al.: LEN for treatment naïve PWH**

**Study Design**

**Treatment naïve N=182**
- Key eligibility criteria:
  - ARV naïve
  - HIV-1 RNA ≥200 copies/mL
  - CD4+ cell count ≥200 cells/μL

**Induction**
- Treatment Group 1
  - LEN SC Q6M
  - F/TAF oral QD
- Treatment Group 2
  - LEN SC Q6M
  - F/TAF oral QD
- Treatment Group 3
  - LEN oral QD
- Treatment Group 4
  - B/F/TAF oral QD

**Maintenance**
- Week 28: TAF oral QD
- Week 54: BIC oral QD

**DMC recommended continuation of study, based on Week 16 results (i.e. abstract data)**

*LEN oral lead-in (600 mg on Days 1 and 2, 300 mg on Day 8) followed by LEN SC 927 mg on Day 15; F/TAF 200/25 mg; †Participants in TG 1 and 2 will need HIV-1 RNA results <50 copies/mL at Wks 16 and 22 to initiate either TAF 25 mg or BIC 75 mg at Wk 28; those with HIV-1 RNA ≥50 copies/mL will discontinue study at Wk 28; ‡LEN 600 mg on Days 1 and 2, followed by LEN 50 mg from Day 3; F/TAF 200/25 mg; §B/F/TAF 50/200/25 mg.*

Gupta et al, OALB03-02211
FDA Snapshot Outcome (ITT) at Week 28

- In the pooled LEN group (receiving either SC [TG 1+2] or oral [TG 3] LEN in combination with F/TAF), 94% (147/157) achieved HIV-1 RNA <50 copies/mL at Week 28.

*1 participant discontinued due to not meeting the protocol criteria of having HIV-1 RNA <50 copies/mL prior to Week 28; 1 participant discontinued on Day 2.

Gupta et al, OALB03-0211
One ppt with emergent resistance at wk 10:

- Capsid: q67H+K70R
- RT: M184M/I

LEN [plasma] at target throughout

Calibrate Study, Gupta et al.: LEN for treatment naïve PWH
Long-acting PrEP: Hillier et al

Islatravir (ISL): oral, monthly, novel class agent: nucleoside reverse transcriptase translocation inhibitor being developed for PrEP
• 2 ppts d/c’d due to AEs – mild, considered to be drug-related

• Common grade 3/4 AEs: transient, asymptomatic – elevated Cr, elevated lipase (no difference in ISL vs placebo)

• Rare (N=1-2) grade 3/4 AEs: AST incr, CK incr, neutropenia.
Treatment of major co-infections (TB & Crypto)


- **ZeNix study** (Conradie et al, A-LB-IAS2021-02405): N=181 M/XDR TB, 20% with HIV. 6M BPa, randomized to 6L1200/2L1200/6L600/2L600. Similar efficacy (6M post-treatment cure, 84-93%) and lower side effects in the lower dose/duration Lz groups

- **Ambition Study** (Lawrence et al, A-LB-IAS2021-02370): induction with single-dose, high-dose AmBisome (liposomal ampho B) + 14d (5FU + fluconazole) was non-inferior to WHO SOC induction (7d (amphoB + 5FU) → 7d fluconazole) for the outcome of all-cause mortality in PWH with cryptococcal meningitis. Ambisome had better safety profile.
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