AETC AIDS Education & Training Center Program Mountain West

IAS 2021 Conference Highlights

Adrienne E Shapiro, MD, PhD
Acting Assistant Professor
Departments of Global Health and Medicine (Allergy and Infectious Diseases)
University of Washington

Last Updated: 22 July 2021

echo

Disclosures

Grant funding: Vir Biotechnology, Inc.

Outline

- 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**)

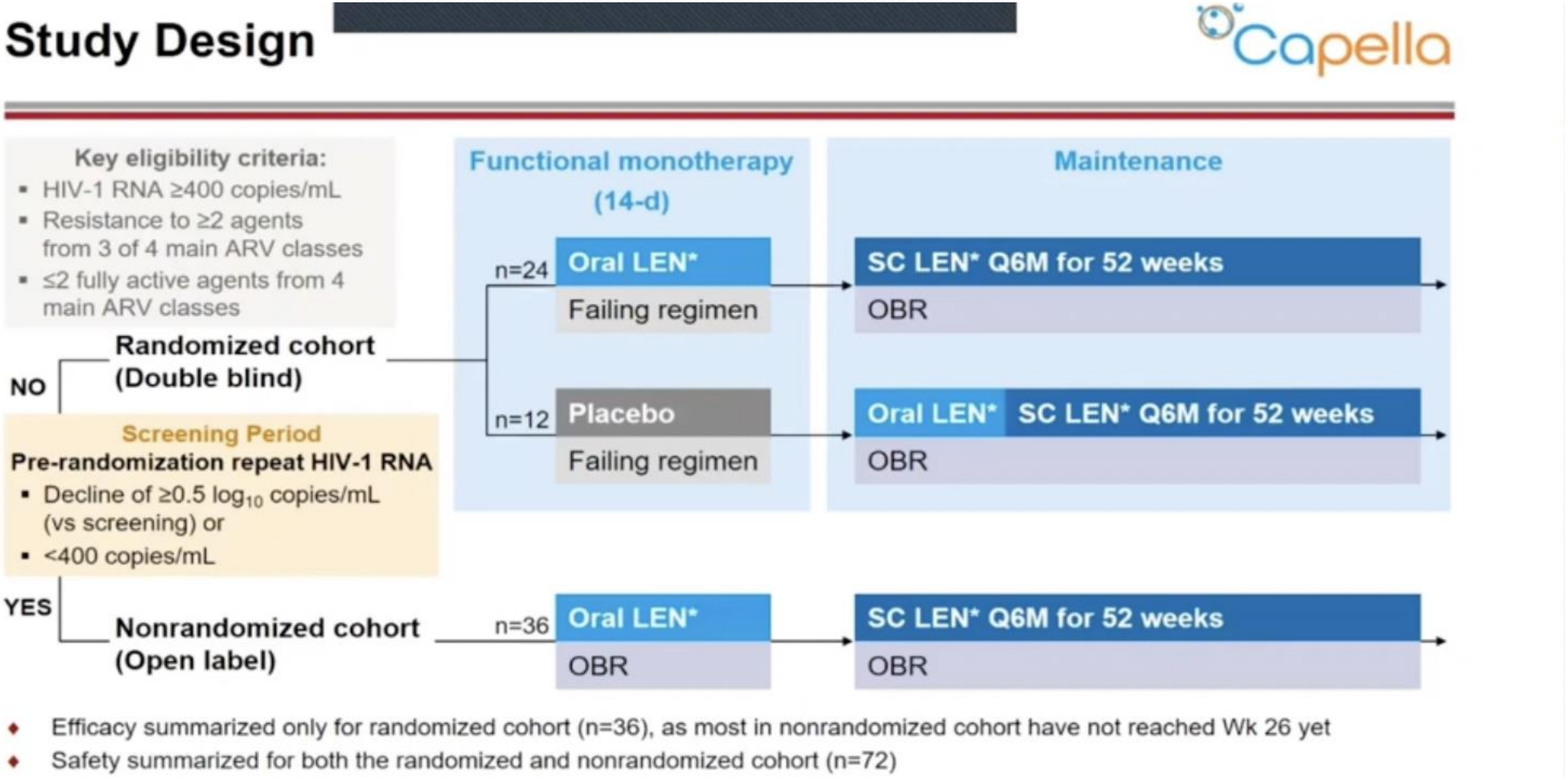
- Long-acting PrEP
- Safety & PK of monthly islatravir – week 24 (A-LB-IAS2021-02361, Hillier et al)

- Co-infection (TB, Cryptococcus) treatment lighting round

MWAETC

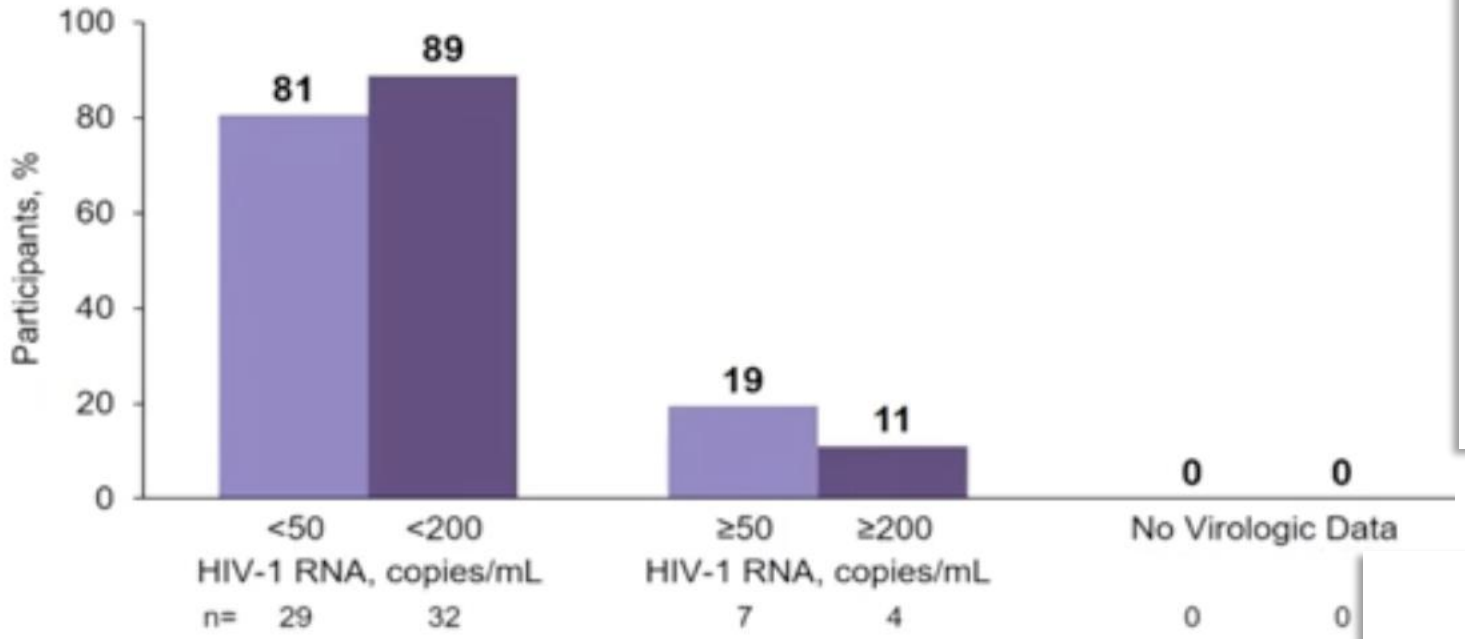
Capella Study, Molina et al.

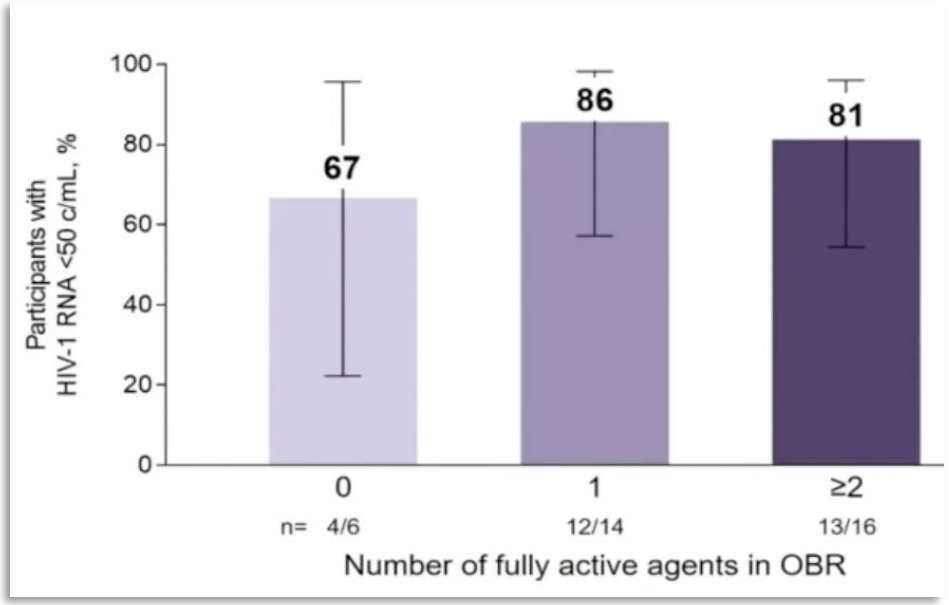
Lenacapavir (LEN): first-in-class HIV capsid inhibitor; *in vitro* data for effect against NRTI, NNRTI, INSTI–resistant HIV→ use for highly treatment-experienced (HTE) PWH



Capella Study: LEN for HTE PWH

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





n (%)	Randomized Cohort n=36
Participants meeting criteria for resistance testing	11 (31)
No emergent LEN resistance	7 (19)
Emergent LEN resistance	4 (11)
M66I	4
Q67H	1
K70N/R/S	1
N74D	1

- All 4 participants with emergent LEN resistance remained on LEN
  - 3 participants re-suppressed at a later visit: 2 without and 1 with OBR change
  - 1 participant with no fully active agent never suppressed (max 1.7 $\log_{10}$ copies/mL decline in HIV-1 RNA)
- No participant developed additional resistance to the agents in the OBR

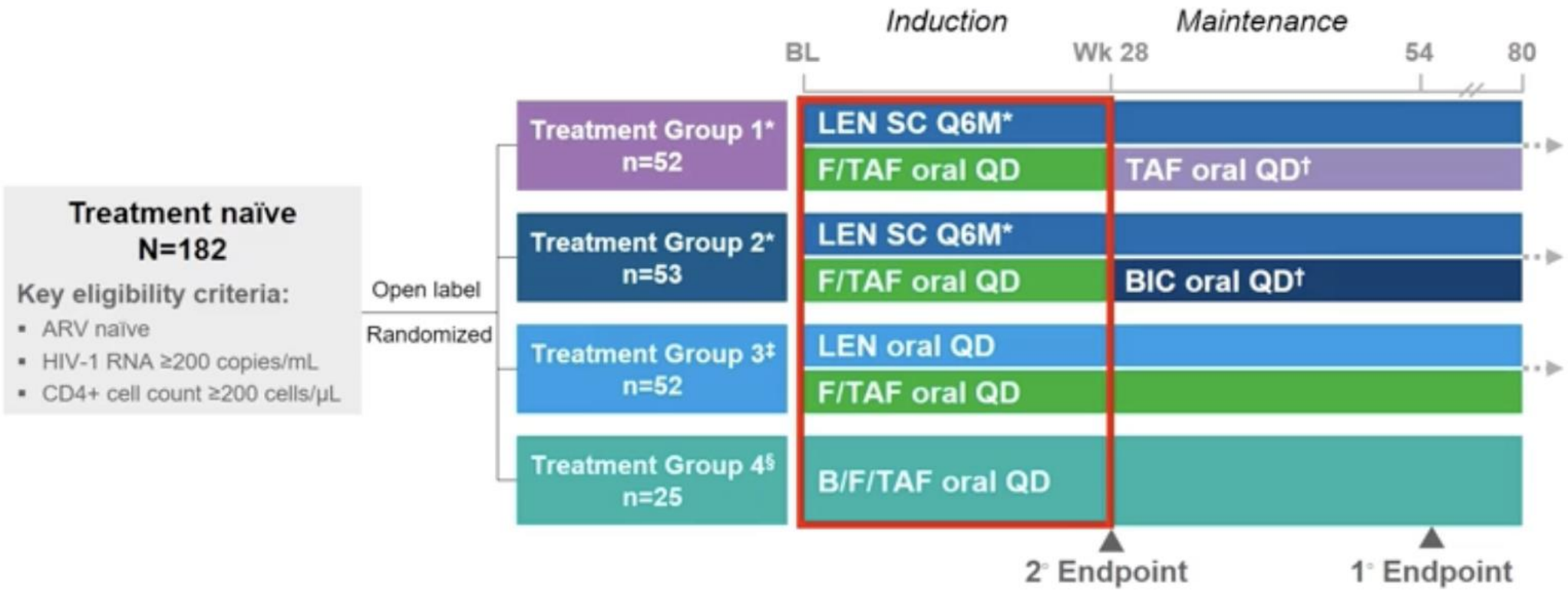
Good safety & tolerability
-no SAEs related to drug or AEs leading to discontinuation
-median CD4 increase 81 over 26 weeks, none <50 at 26wk

Molina et al, A-LB-IAS2021-02605

MWAETC

Calibrate Study, Gupta et al.: LEN for treatment naïve PWH

Study Design



- 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.
ARV, antiretroviral; BIC, B, bictegravir; BL, baseline; DMC, data monitoring committee; QD, once daily; Q6M, every 6 months; TG, treatment group; Wk, Week.

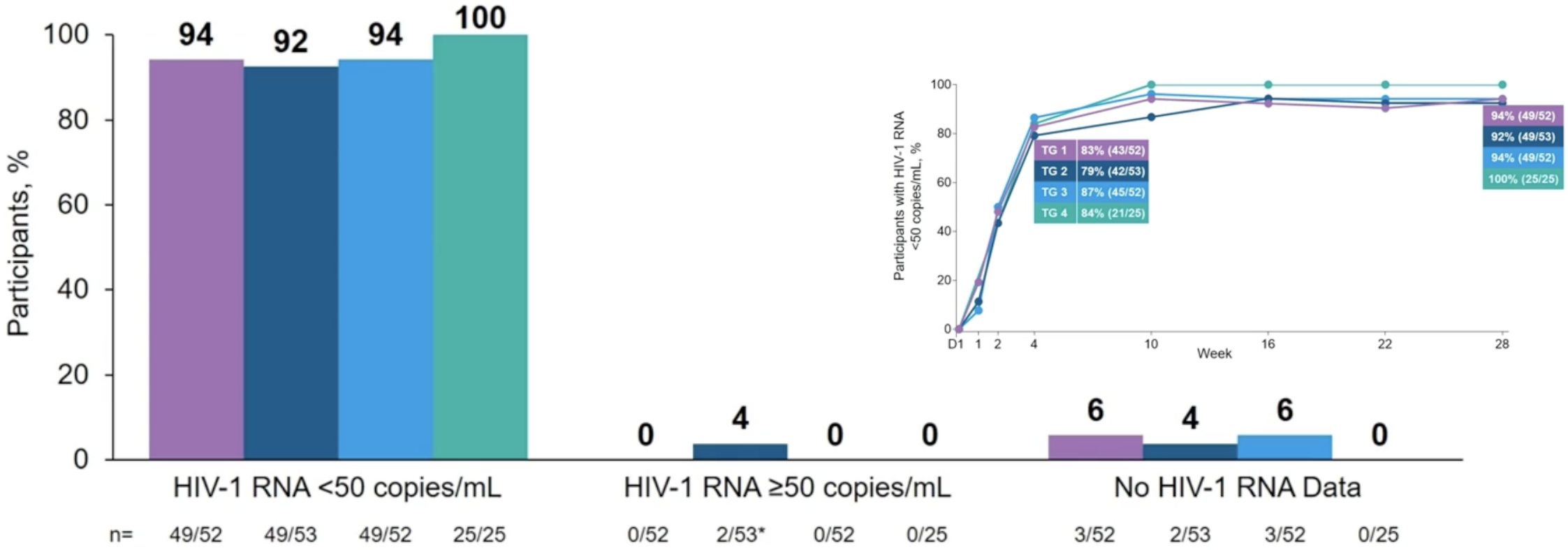
Gupta et al, OALB03-02211

Calibrate Study, Gupta et al.: LEN for treatment naïve PWH

FDA Snapshot Outcome (ITT) at Week 28

Calibrate

TG 1: LEN SC + F/TAF (→TAF)
TG 2: LEN SC + F/TAF (→BIC)
TG 3: LEN QD + F/TAF
TG 4: B/F/TAF



- 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

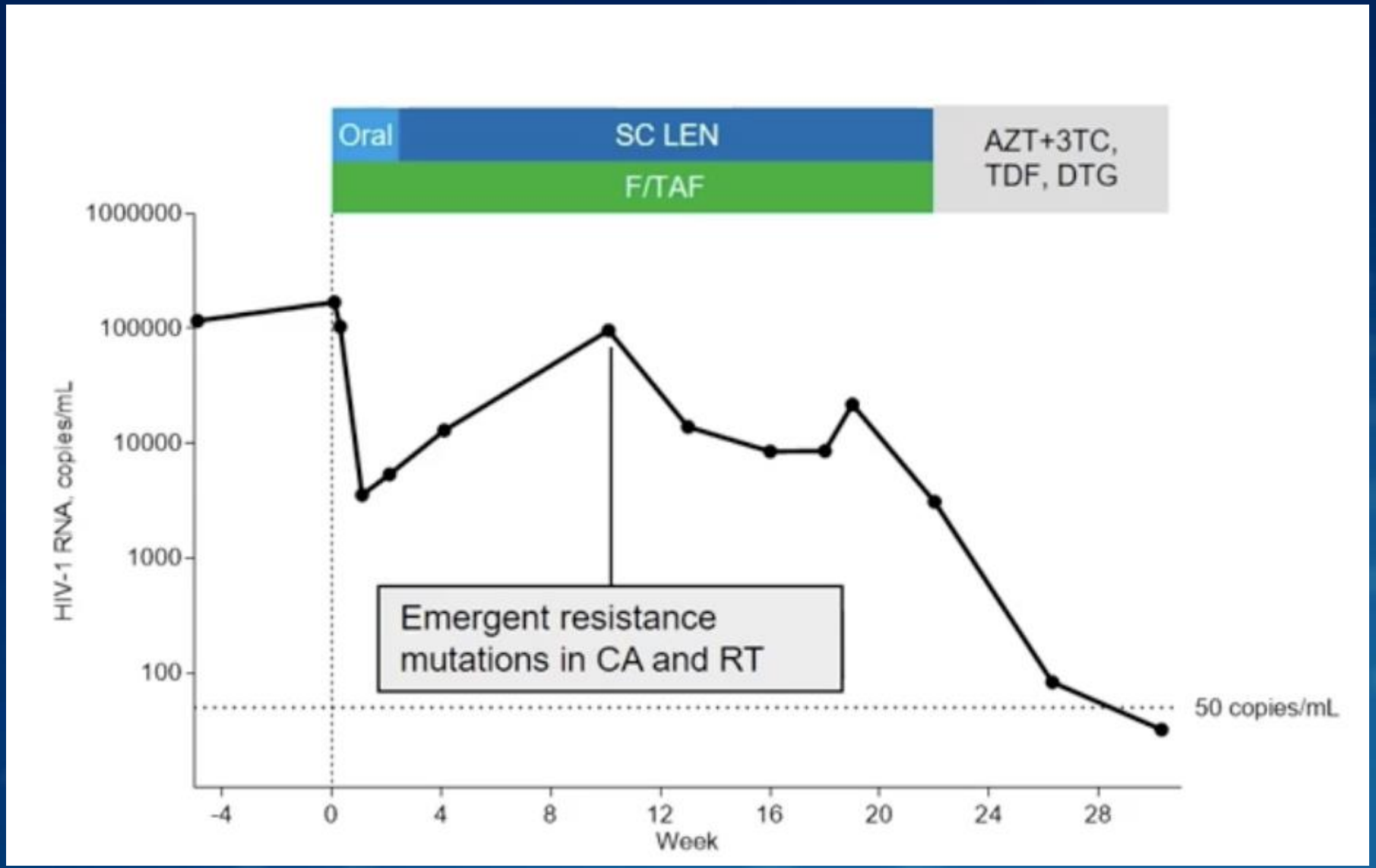
MWAETC

Calibrate Study, Gupta et al.: LEN for treatment naïve PWH

One ppt with emergent resistance at wk 10:

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

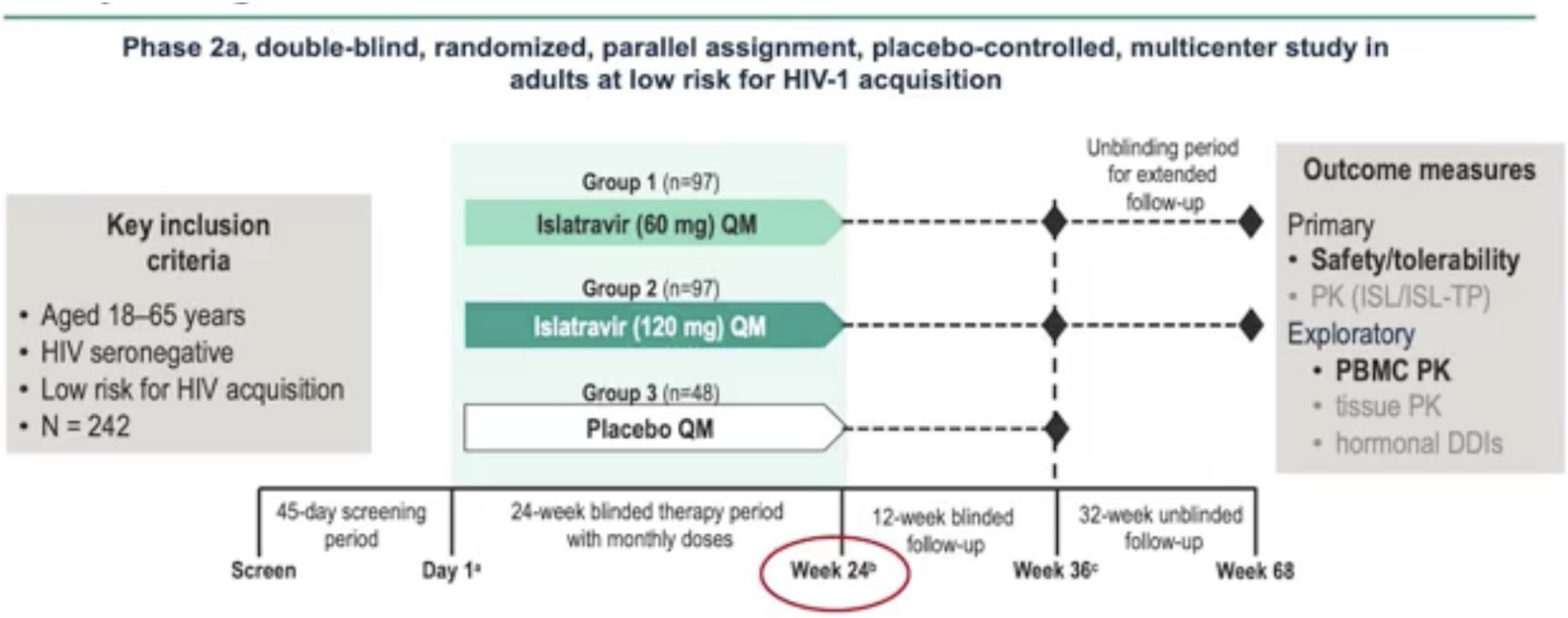
LEN [plasma] at target throughout



Gupta et al, OALB03-02211

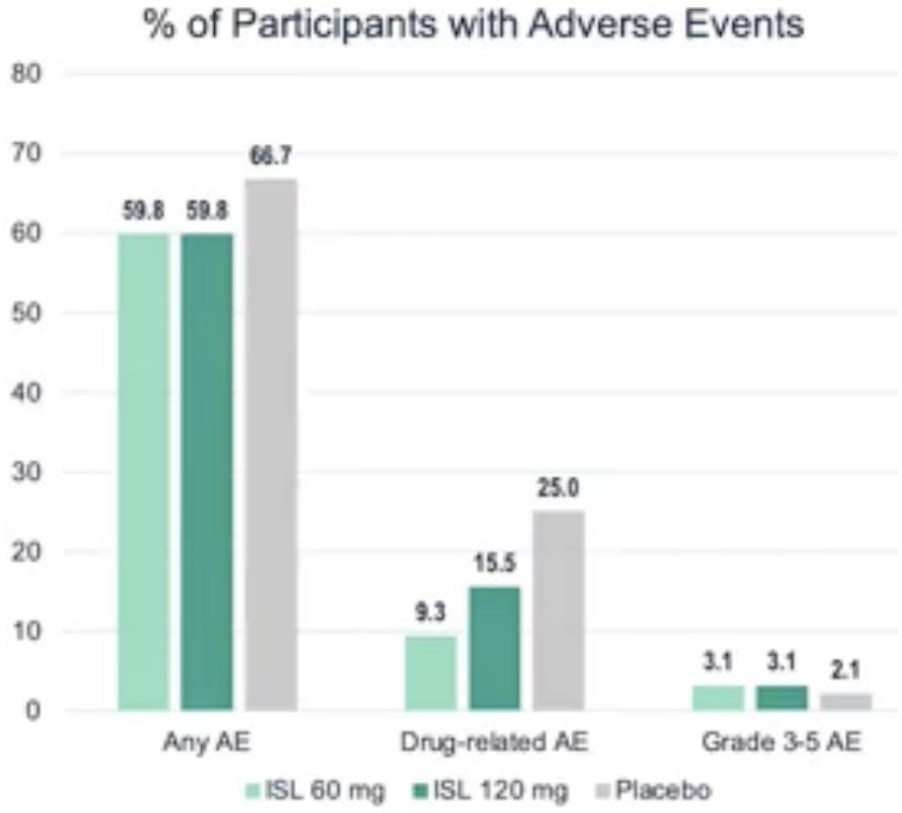
Long-acting PrEP: Hillier et al

Islatravir (ISL): oral, monthly, novel class agent: nucleoside reverse transcriptase translocation inhibitor being developed for PrEP



[a]Randomization to study intervention at Day 1 and stratified by sex (female, male) and region (Africa, non-Africa). [b]Sponsor unblinded at Week 24 to allow for an interim evaluation of safety. Participants and investigators/clinical-site personnel remain blinded up to Week 36. [c]After Week 36, only participants in the PBMC/PK Bridging Subset who were randomly assigned to receive ISL will have an additional 32-week extended, unblinded PK follow-up through Week 68. NCT04003103 (P016).

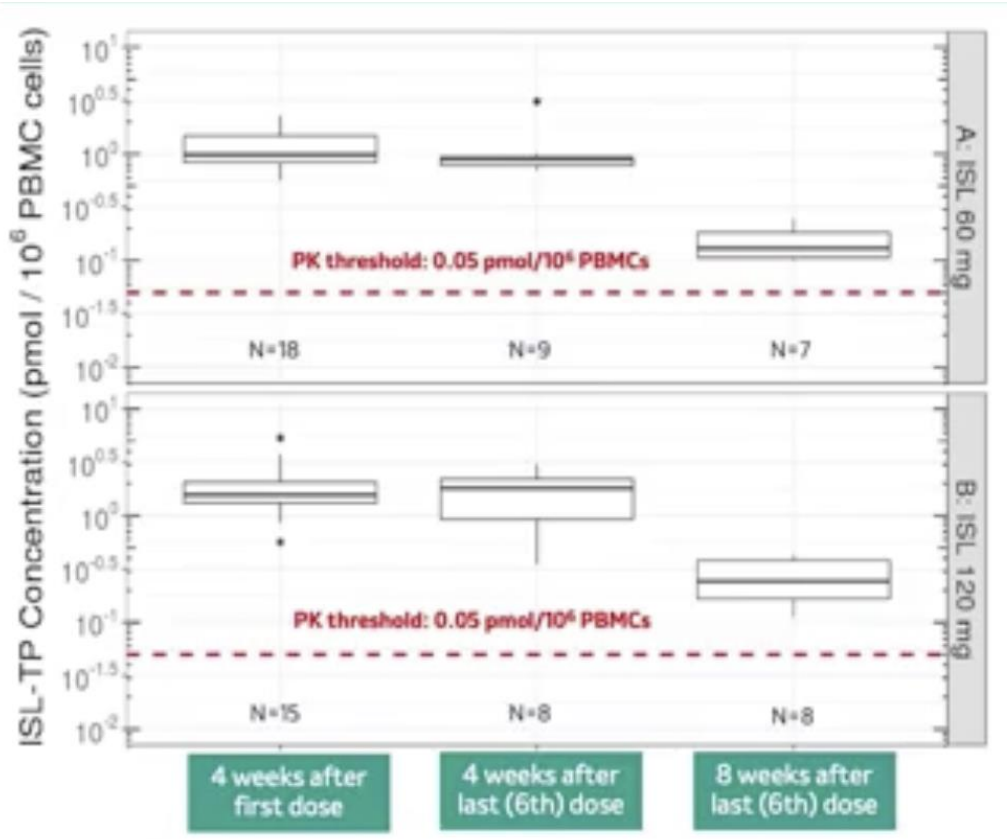
A-LB-IAS2021-02361, Hillier et al



- 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.

Pharmacokinetics of ISL



A-LB-IAS2021-02361, Hillier et al

Treatment of major co-infections (TB & Crypto)

- **TB-Practecal study (Motta et al, A-LB-IAS2021-02458):** BPaL+Mfx vs. SOC for MDR-TB. N=552 randomized in adaptive trial, 25% with HIV. N=120 rdm to BPalMfx, N=122 SOC. DSMB terminated randomization for lack of equipoise, favoring BPaLMfx. Multiple discontinuations, 5 deaths in SOC arm drove difference.
- **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.

MWAETC

Acknowledgment

The Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $2,886,754 with 0% financed with non-governmental sources.

AETC AIDS Education & Training Center Program Mountain West