UNC
INSTITUTE FOR GLOBAL HEALTH
& INFECTIOUS DISEASES

AIDS 2024

AIDS 2024, the 25th International AIDS Conference

A NATAP UPDATE

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IAS 2024: What Matters Most

UNC SCHOOL OF MEDICINE

HIV PREVENTION

- PURPOSE 1 – LEN PrEP in cis-women in S Africa & Uganda.
- HPTN 084 – CAB PrEP in pregnancy
- HPTN 083 – Viral load test predictive value
- Low rates of HIV Testing Prior and During CAB PrEP

HIV TREATMENT

- BEYOND – CAB/RPV effectiveness and satisfaction in clinical practice
- IMPAACT 2017 – CAB/RPV switch in adolescents (global)
- SOLAR-3D – DTG/3TC in treatment experienced but suppressed
- DYAD – DTG/3TC switch from BFTAF – 96-week data
- PASO-DOBLE – DTG/3TC vs BFTAF
- More Artistry-1 data – Oral BIC+LEN switch
- VH184 – 3rd Generation INSTI

HIV COMPLICATIONS

- Reprieve Trial – ABC and MACE
- AFRICOS – HTN and DTG
- Anal Cancer Screening – Mt Sinai data
- DOXYVAC – 96-week data on resistance
- Multi-morbidity in older PWH in US South

COVID-19

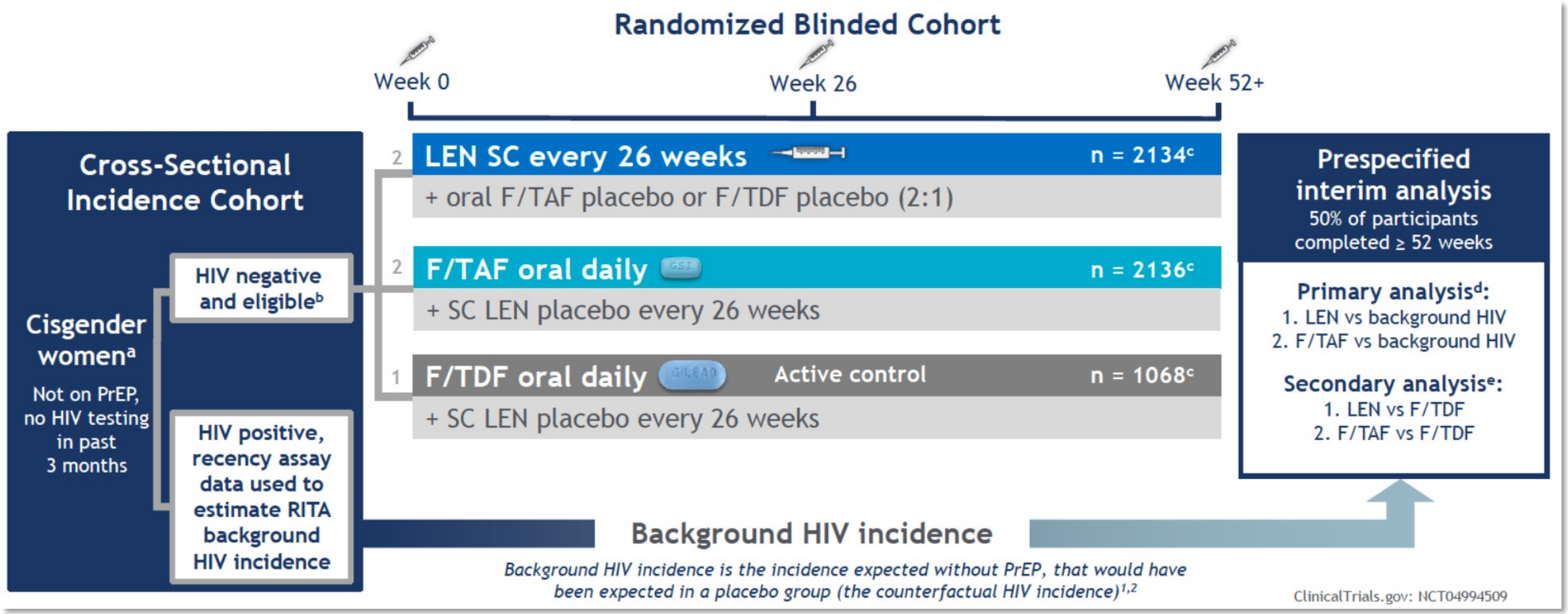
- Circulating variants now
- Vaccination update soon

MPOX

- Clade 1 resurgence
- PALM 007 - TPOXX efficacy
- Vaccination

HIV Prevention

PURPOSE 1: Twice-Yearly LEN Injections vs Daily Oral Tenofovir as PrEP in Cisgender Women



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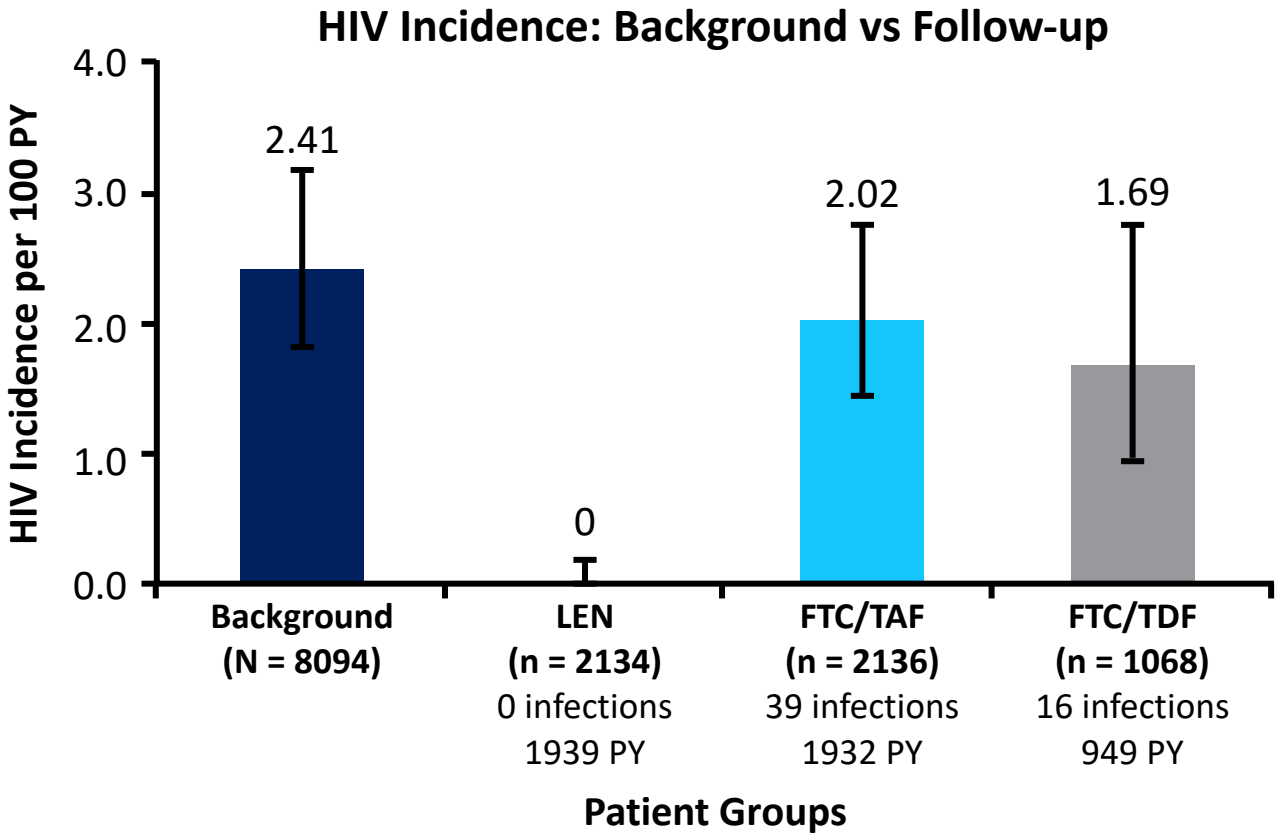
PURPOSE 1: HIV Incidence in mITT Population at Interim Analysis



- At baseline, median age 21 yr, 23%-56% aged 16-18 yr, ~25% with any STI

Comparison	HIV Incidence Rate Ratio (95% CI)*	*P* Value
LEN vs background HIV incidence	0 (0.00-0.04)	<.001
FTC/TAF vs background HIV incidence	0.84 (0.55-1.28)	.21
LEN vs FTC/TDF HIV incidence	0 (0.00-0.10)	<.001
FTC/TAF vs FTC/TDF HIV incidence	1.20 (0.67-2.14)	--

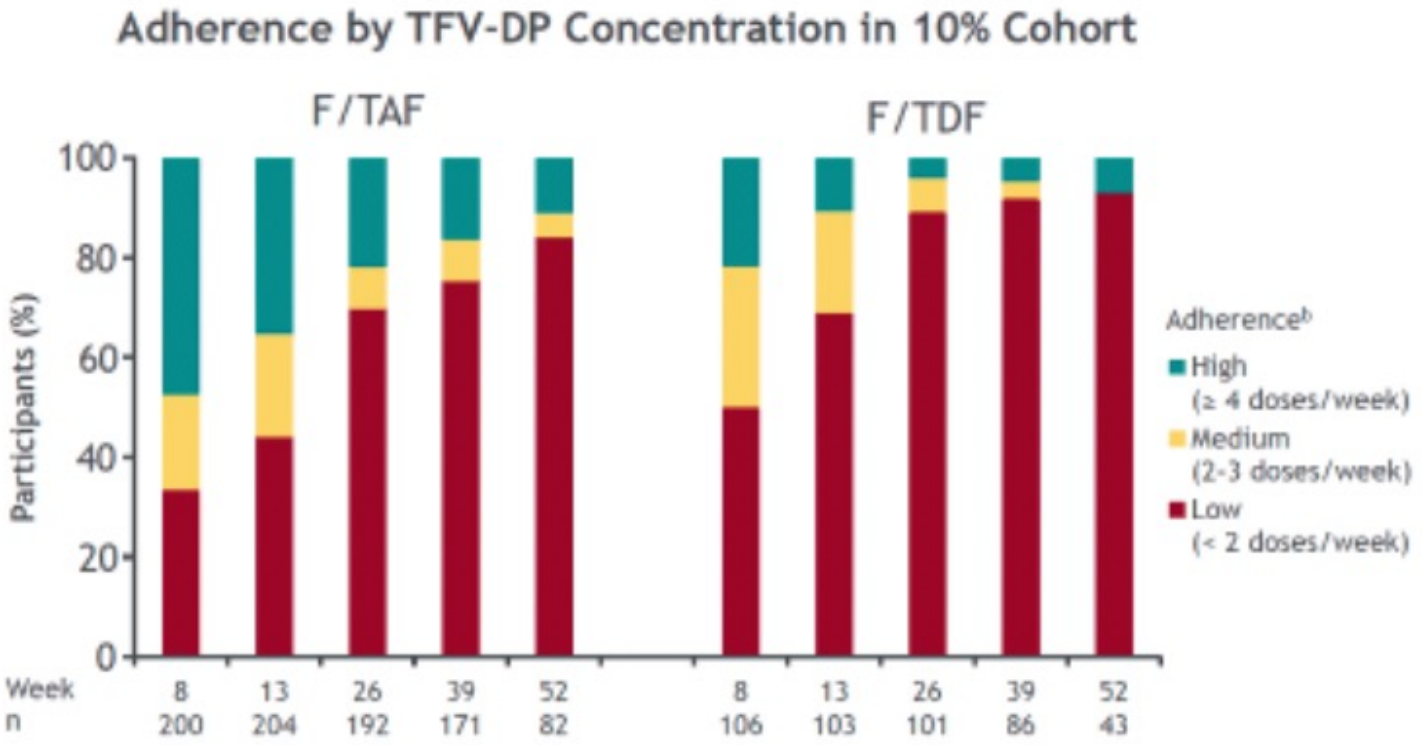
*People found to have HIV at study entry excluded from analysis.

- **Zero HIV infections occurred in cisgender women receiving LEN**
- In oral FTC/TAF arm, HIV incidence no different from background and **treatment adherence was poor**

Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

PURPOSE 1: Treatment Adherence and ISRs

- Injections given on time in
  - 91.5% (4545/4967) at Wk 26
  - 92.8% (2025/2181) at Wk 52
- On-time injection rate similar for LEN and placebo
- **Adherence to oral tablets was low** based on TDF-DP concentration for both FTC/TAF and FTC/TDF, declined over time
- Pregnancies were common and outcomes were similar to those expected for the population



- Among 25,329 injections, 4 ISRs led to treatment discontinuation

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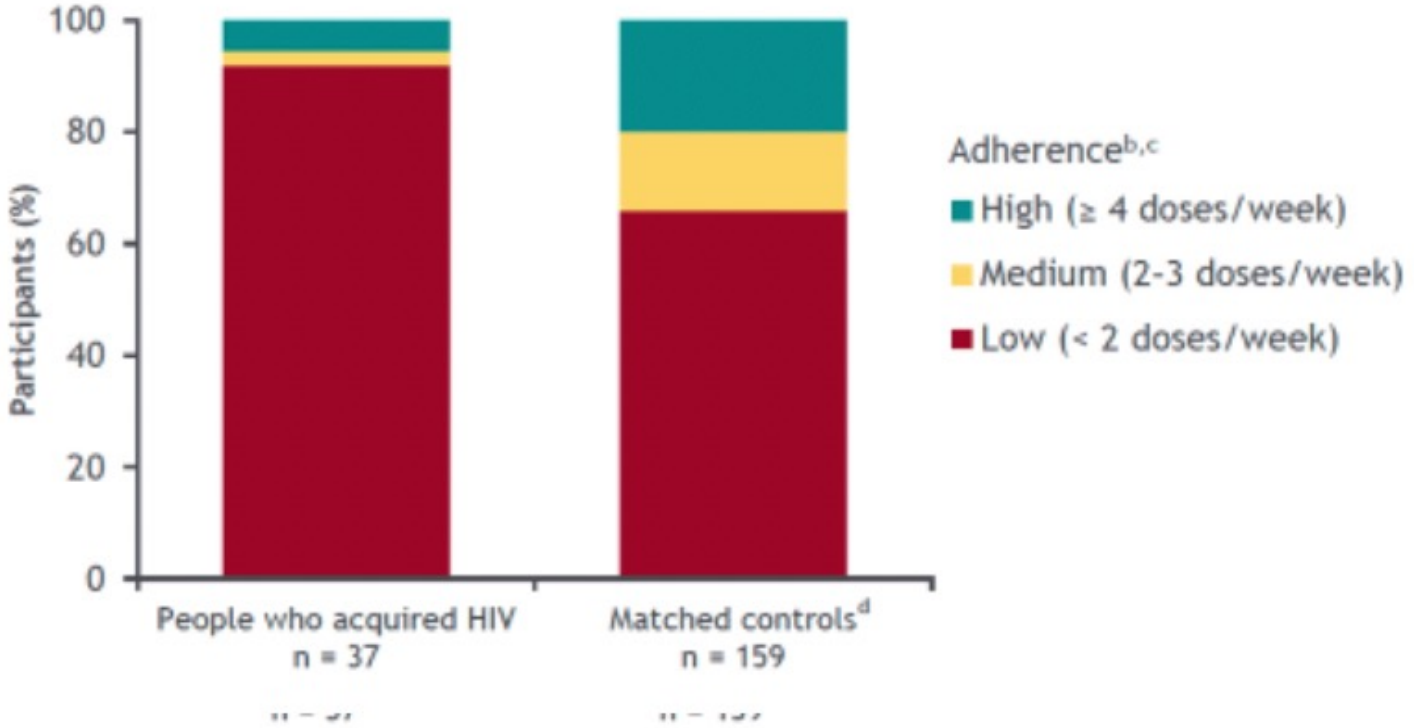

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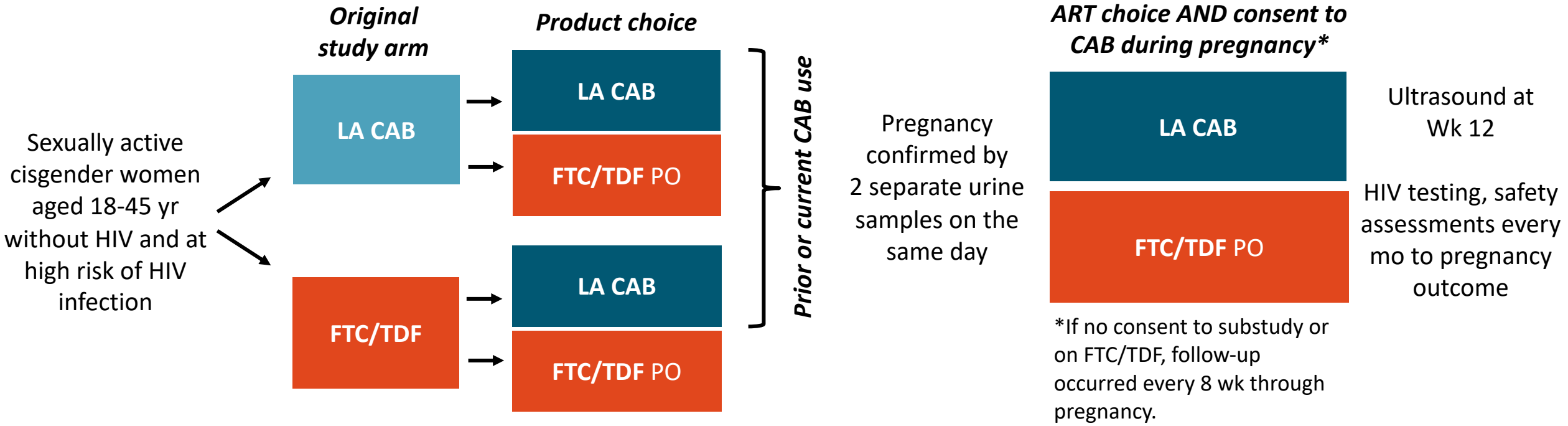
PURPOSE 1 Next Steps

Bekker. AIDS 2024. Abstr SS0407.

HPTN 084 Open-Label Extension: Safety Evaluation of LA CAB During Pregnancy

- International, randomized, double-blind phase III trial, with evaluation of OLE in pregnant individuals offered the choice of LA CAB or FTC/TDF from 2022 onwards



- **Primary outcomes:** pregnancy incidence, maternal AE incidence, individual and composite pregnancy outcomes: birth including spontaneous abortion <20 wk or IUFD; stillbirth ≥20 wk or premature birth <37 wk or small gestational age; infant outcomes

Delany-Moretlwe. AIDS 2024. Abstr SY2503. NCT03164564.

Slide credit: clinicaloptions.com

OLE participant disposition

HPTN HIV Prevention Trials Network

From start of OLE until 31 DEC 2023

2472 participants
joined the OLE

410 participants
had ≥ 1 pregnancy recorded

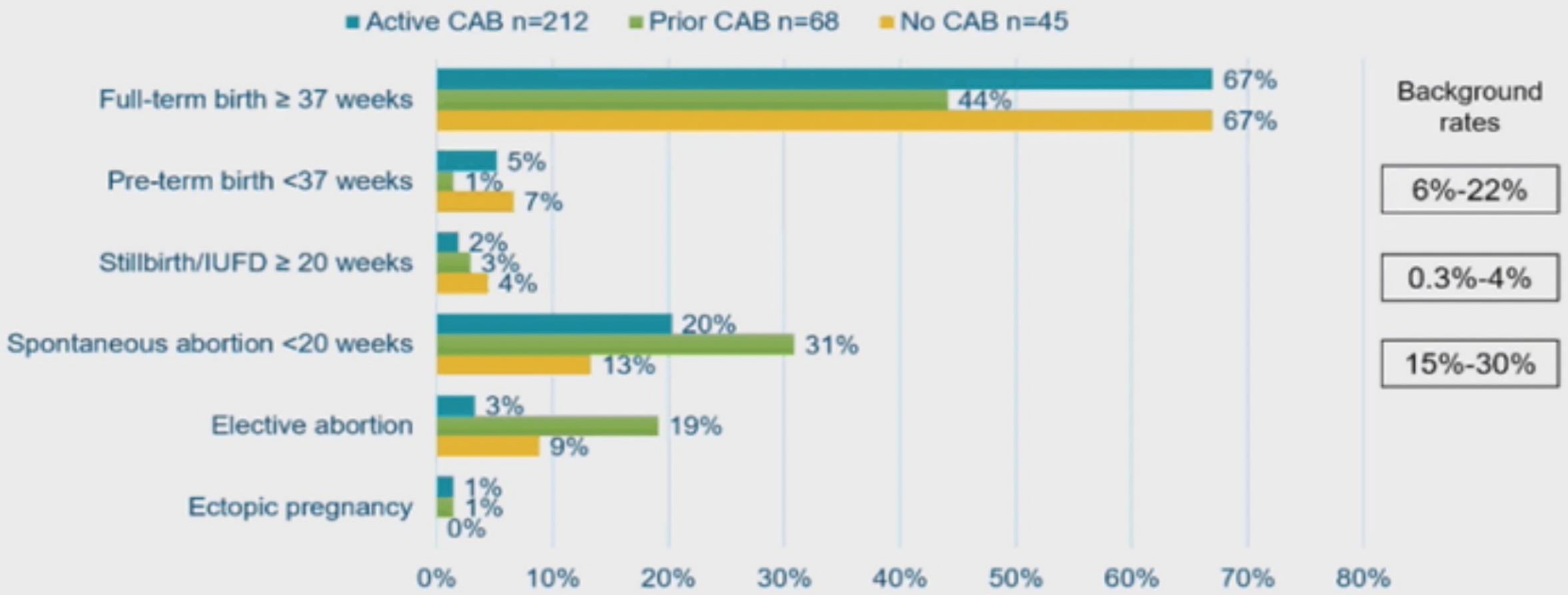
312 participants
had ≥1 pregnancy with a recorded outcome

325 pregnancies with recorded outcome included in safety analysis
(n=64 pregnancies at time of OLE start, n=261 incident pregnancies)

320 pregnancies with 1 outcome
5 pregnancies with 2 outcomes

Delany-Moretlwe. AIDS 2024. Abstr SY2503. NCT03164564.

OLE pregnancy outcomes, by exposure



www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit/data-harmonization; Balkus, PLoS One 2021

Delany-Moretlwe. AIDS 2024. Abstr SY2503. NCT03164564.

Separate PK study from HPTN 084 showed trough levels >4x IC_{90} in 98%

HPTN 083: HIV-1 RNA Screening in Cisgender Men and Transgender Women Receiving LA CAB for PrEP

- In original HPTN083 PrEP study, in both LA CAB and FTC/TDF arms, HIV detection with antigen/antibody testing was delayed vs with qualitative HIV-1 RNA testing[2-3]

Delays in Diagnosis, Median Days[3]	Baseline Infections	Incident Infections
LA CAB for PrEP	62	98
Oral FTC/TDF for PrEP	34	31

- Based on these results, 2021 CDC guidelines recommend HIV-1 RNA assays to monitor people on oral or LA injectable PrEP[4]
- Current analysis of OLE participants (LA CAB only) through November 30, 2023, calculated positive predictive value and false positive rates of isolated positive RNA results and assessed screening sensitivity[1]

1. Landovitz. AIDS 2024. Abstr OAE0406LB. 2. Marzinke. CROI 2021. Abstr 153. 3. Marzinke. J Infect Dis. 2021;224:1581.
4. cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf.

HPTN 083: HIV-1 RNA Testing Results

- Out of **26,528 HIV-1 RNA tests**, **22 were false positives**
  - Of these, 7 resulted in subsequent LA CAB administration delays
- A single, isolated positive HIV-1 RNA test result was uncommon, but when it occurred, was frequently a false positive

Results From Isolated Positive HIV-1 RNA Tests

Patient Group	PPV, % (95% CI)	False Pos Rate, % (95% CI)
Overall	18.5 (7.0-38.7)	0.08 (0.05-0.13)
No LA CAB in last 6 mo	60 (17-92.7)	0.06 (0.01-0.25)
LA CAB in last 6 mo	9.1 (1.6-30.6)	0.09 (0.05-0.14)

- HIV-1 RNA assay performed better in those who had not received LA CAB in the past 6 mo

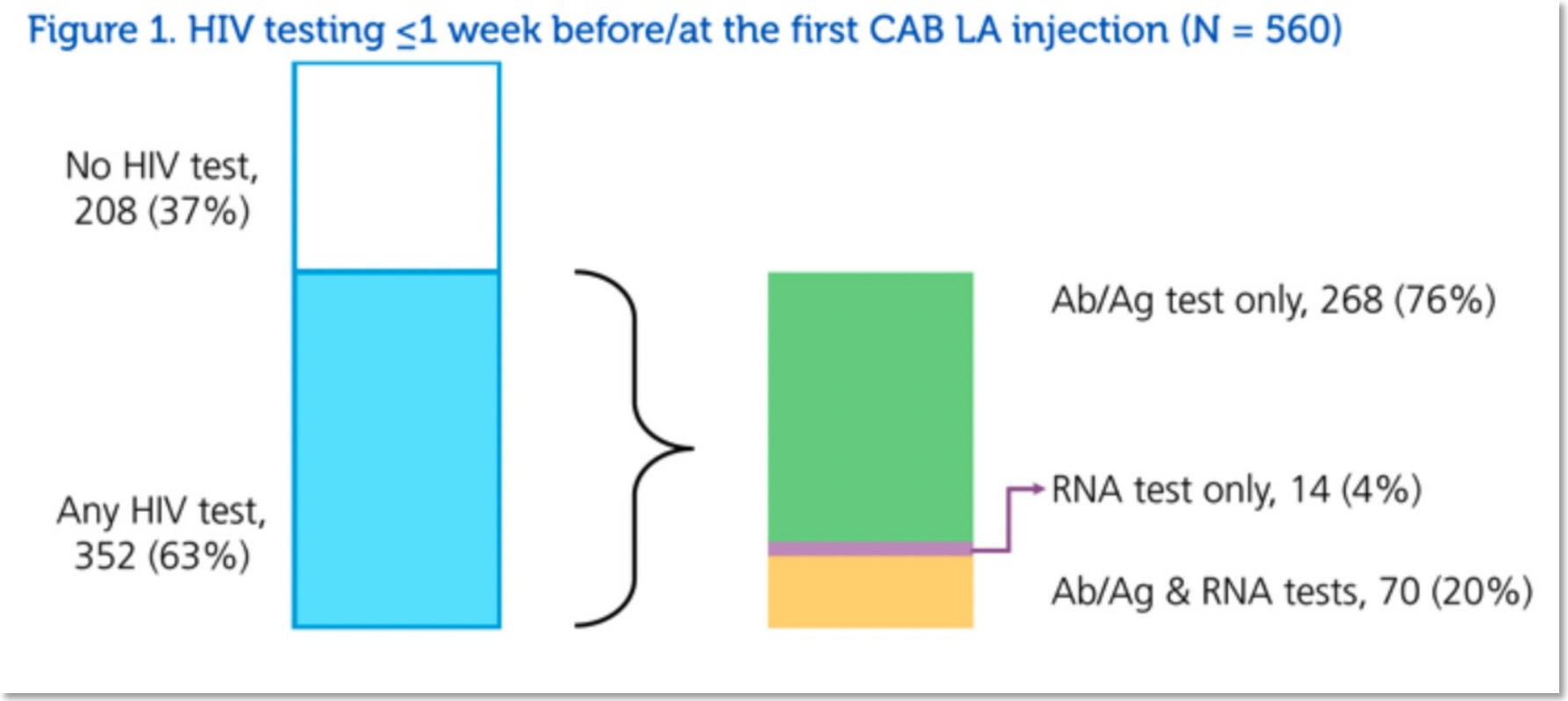
- **Repeat HIV-1 RNA testing can clarify whether the initial positive result is indeed an HIV infection**

Landovitz. AIDS 2024. Abstr OAE0406LB.

Slide credit: clinicaloptions.com

HIV Testing during CAB PrEP – Opera Cohort

- CDC guidelines and CAB package insert indicate HIV testing before CAB PrEP initiated and at time of each injection visit.
- OPERA Cohort (1M people at 103 clinics in US): Among 560 CAB PrEP users, HIV testing within 1 week and within 4 weeks prior to injection assessed.



Hsu. AIDS 2024. .

HIV Testing during CAB PrEP – Opera Cohort

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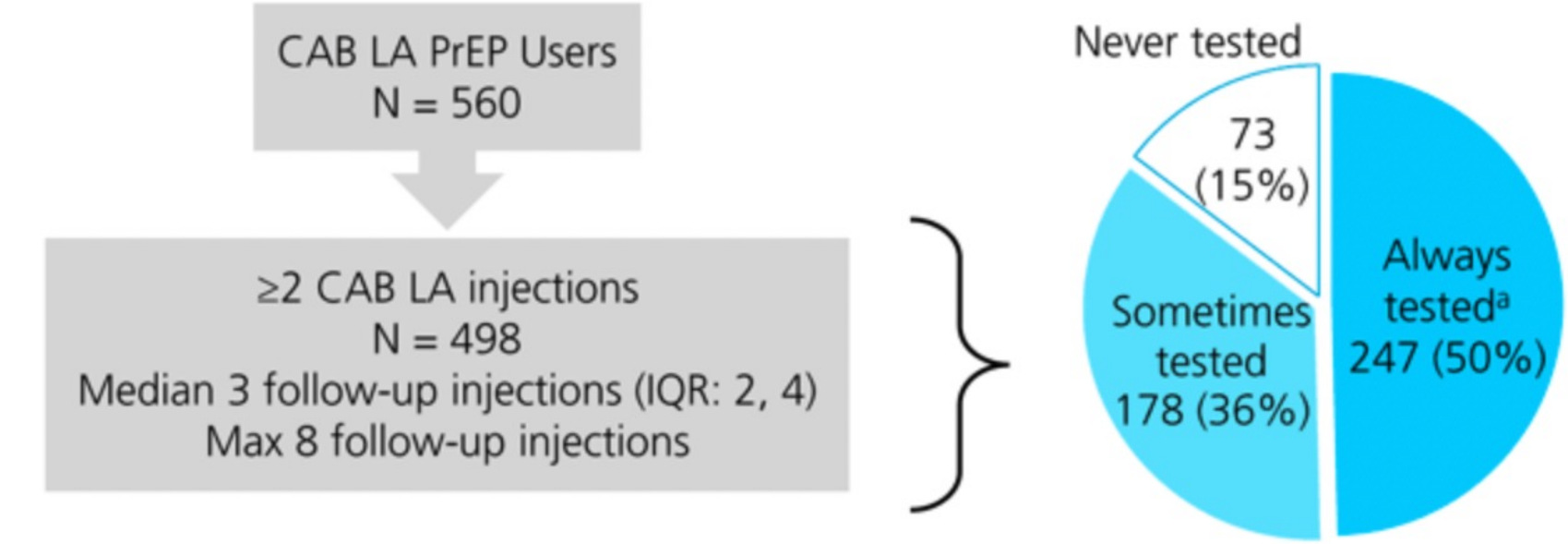
Figure 2. CAB LA PrEP users with ≥2 injections and frequency of HIV testing ≤1 week before/at each follow-up injection



[a] 29 individuals (6%) received both Ag/Ab and RNA tests at each follow-up injection

Hsu. AIDS 2024. .

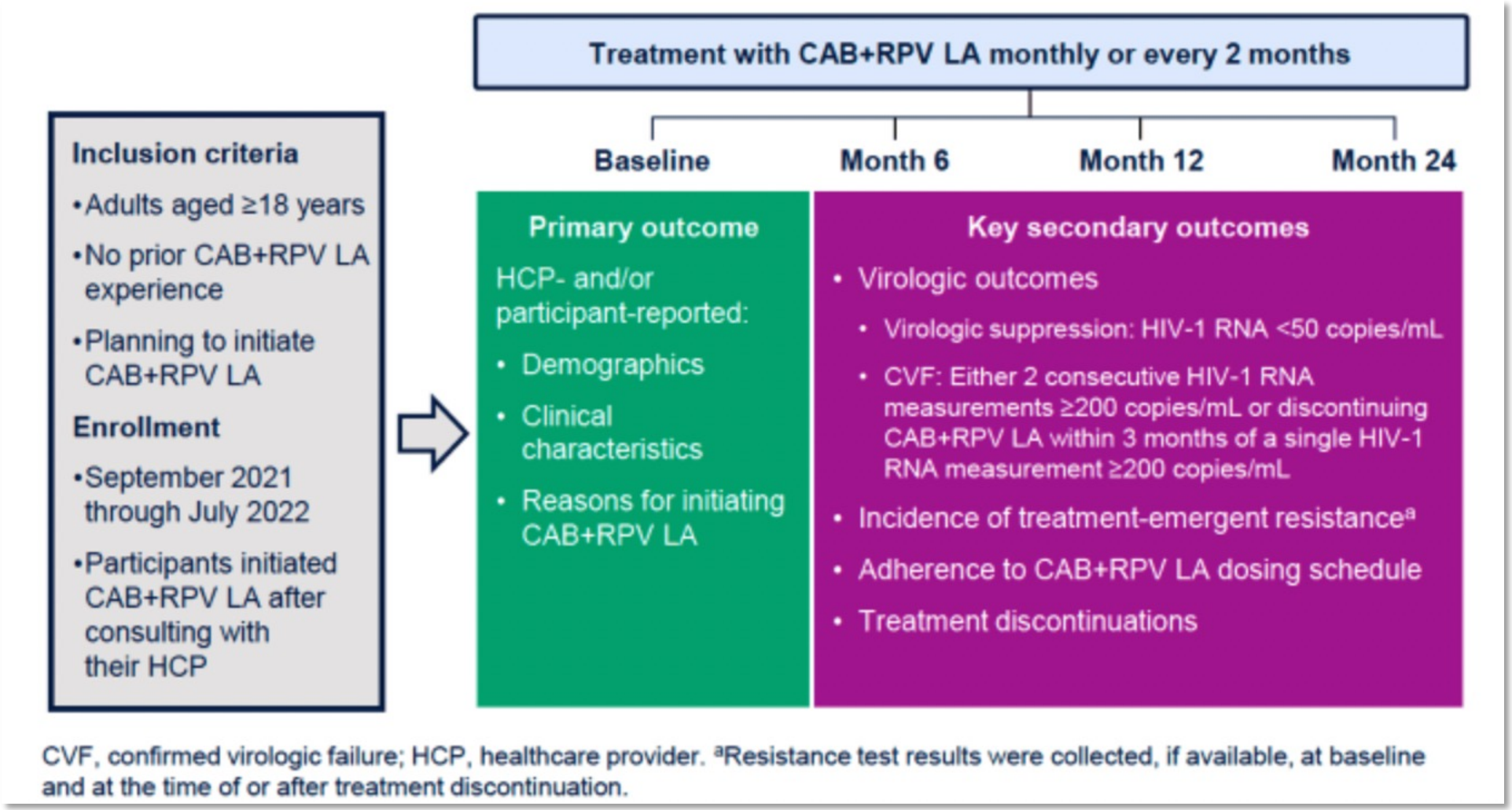
Why does this matter? HIV Prevention

- **Lenacapavir** as an every 6-month subcutaneously injection is progressing to become a major advance in HIV prevention. Clinical trials data continue to show greater adherence to injected PrEP and user preference data strongly supports semi-annual PrEP option.
- The currently approved injectable PrEP, **cabotegravir**, is safe in pregnancy.
- **Viral load** as a screening test for people on CAB PrEP, had very low positive predictive value, especially for those adherent/taking to CAB with most isolated detected results being false.
- However, in clinical practice, there may be **suboptimal HIV testing** before and during CAB PrEP, risking missed infections.

HIV Treatment

CAB/RPV Effectiveness and satisfaction

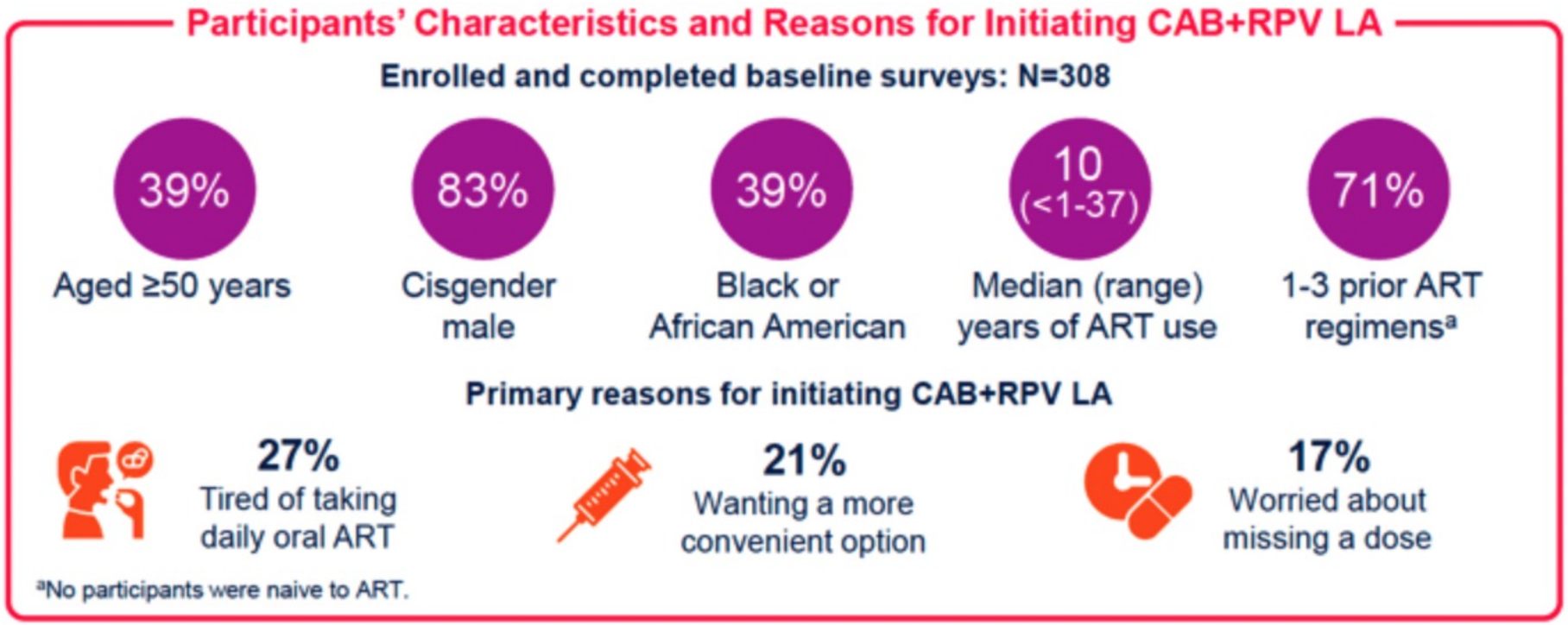
- **BEYOND Study** – Pragmatic study design, 27 US clinics.



Schneider. AIDS 2024. .

CAB/RPV Effectiveness and satisfaction

- 308 patients initiated CAB/RPV
  - 272 completed 12-month follow-up
    - 75 designated users Inconsistent with the Label (not suppressed at start, prior resistance, prior failure)



- 91% on time injections

Schneider. AIDS 2024. .

CAB/RPV Effectiveness and satisfaction

Table 2. Virologic Outcomes Observed at Month 6 and Month 12 Based on Most Recent Viral Load

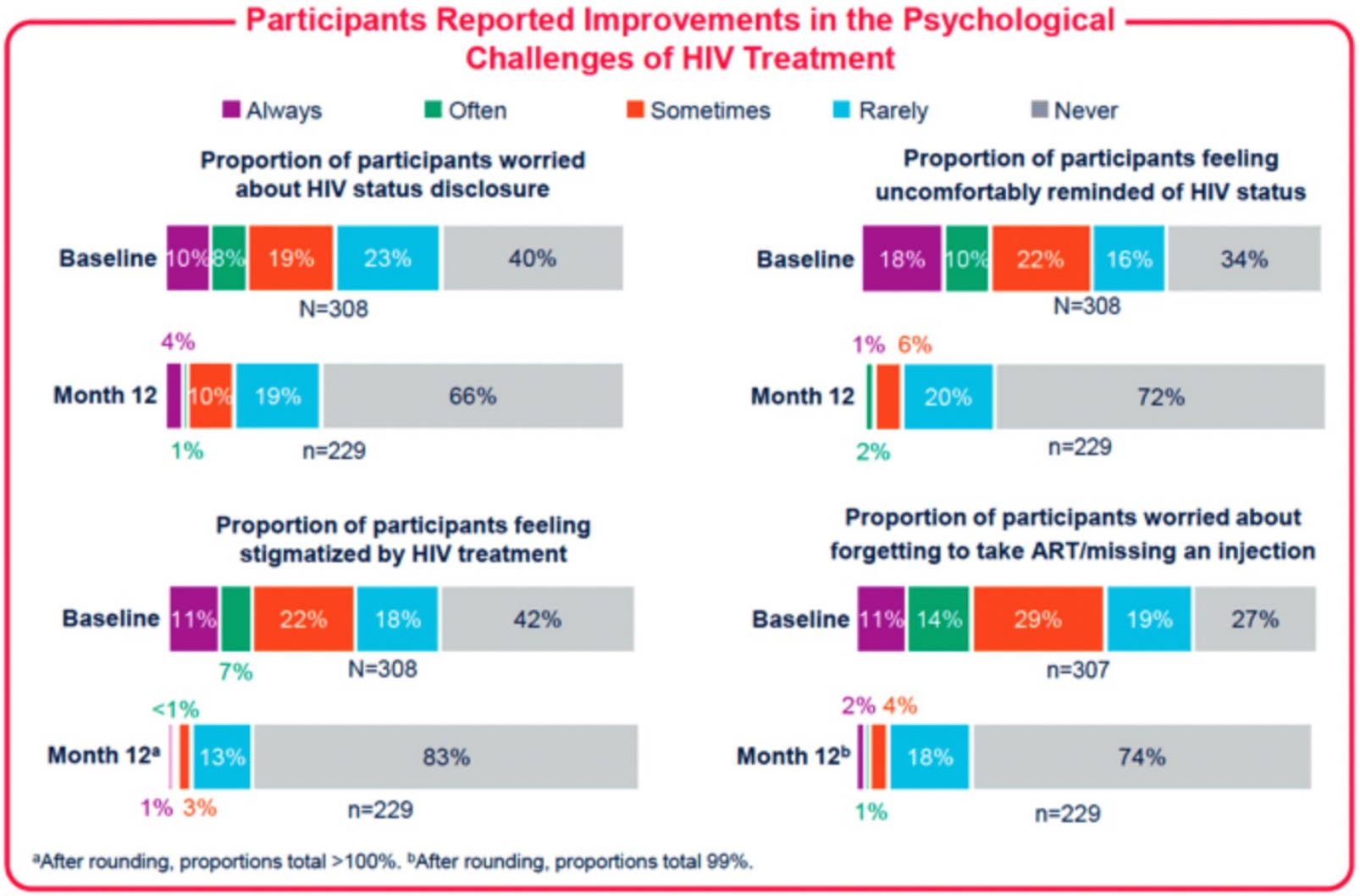
Category	Month 6			Month 12[a]		
	CWL (N=233)	IWL (N=75)	Total (N=308)	CWL (N=210)	IWL (N=62)	Total (N=272)
Total participants with viral load data at both baseline and respective time point, n[b]	206	60	266	156	44	200
Participants with baseline viral load <50 copies/mL, n[b]	206	42	248	156	31	187
<50 copies/mL, n (%)	198 (96)	37 (88)	235 (95)	153 (98)	28 (90)	181 (97)
≥50 copies/mL, n (%)	8 (4)	5 (12)	13 (5)	3 (2)	3 (10)	6 (3)
Participants with baseline viral load ≥50 copies/mL, n[b]	0	18	18	0	13	13
<50 copies/mL, n (%)	NA	17 (94)	17 (94)	NA	13 (100)	13 (100)
≥50 copies/mL, n (%)	NA	1 (6)	1 (6)	NA	0	0
CVFs, n (%)[c]	2 (1)	4 (5)	6 (2)	0	1 (2)	1 (<1)

CVF, confirmed virologic failure; NA, not applicable. [a]Population with ≥1 viral load test between Month 6 and 12. [b]Based on most recent viral load test. [c]Proportions calculated using total N for each column. Cumulative CVFs through Month 12: 7/308 (2%) overall; 2/233 (1%) CWL; 5/75 (7%) IWL.

Schneider. AIDS 2024. .

CAB/RPV Effectiveness and satisfaction

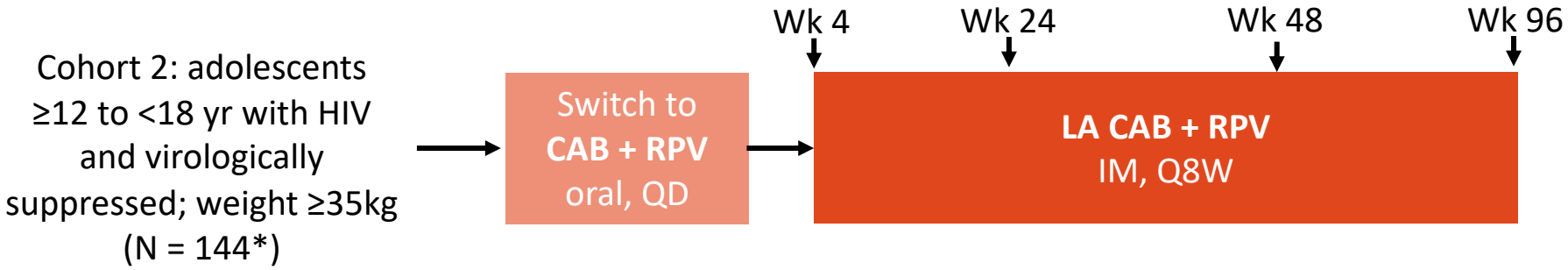
- Through Month 12, 40 participants had **discontinued** CAB+RPV LA (CWL, n=27; IWL, n=13). The most common HCP-reported reasons for discontinuation were:
  - Medication cost or access issues
  - Patient preference
  - ISRs or injection pain
  - "Other"



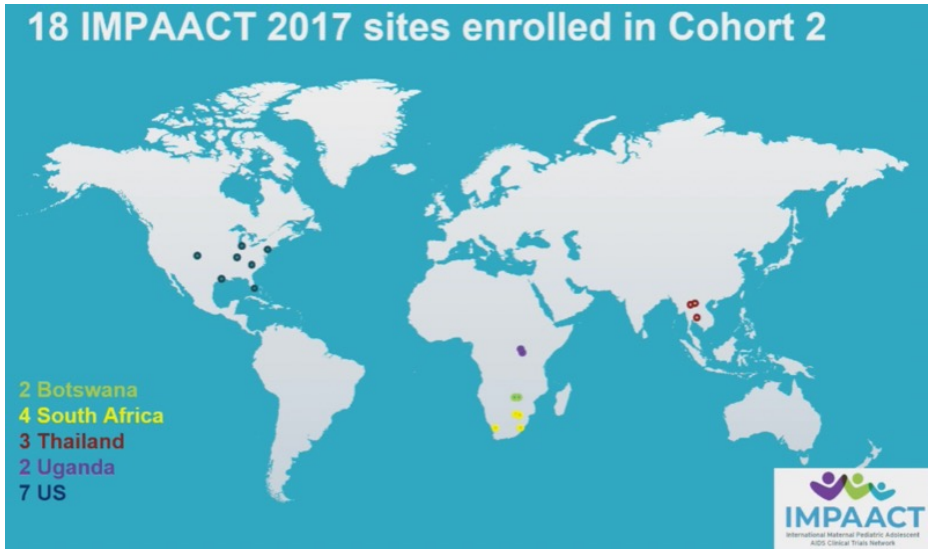
Schneider. AIDS 2024. .

IMPAACT 2017/MOCHA: Switch to LA CAB + RPV in Adolescents With HIV

- Multicenter, open-label, noncomparative phase I/II study
  - Cohort 2 enrolled at 18 global sites including US, Uganda, Botswana, South Africa, Thailand



- **Primary outcome**: safety (adverse events, deaths) through Wk 24
- **Secondary outcomes**: pharmacokinetics, plasma HIV-1 RNA levels, number of participants with virologic failure, and adverse events through Wk 48



NCT03497676. impaactnetwork.org/studies/impaact2017. Gaur. AIDS 2024. Abstr OAB2606LB.

IMPAACT 2017/MOCHA: Safety, Virologic Efficacy, PK, and Participant Experience Through Wk 48

- **Wk 48 virologic success per FDA snapshot: 97.2%**
  - All with Wk 48 assessment (n = 140) had HIV-1 RNA <50 c/mL
- **No cases of CVF** (2 consecutive HIV-1 RNA ≥200 c/mL)
- Median pre-dose CAB and RPV concentrations at Wk 48 approximated those in adults and were above respective protein-adjusted IC_{90}

All 140 participants who responded to Wk 48 Preference Questionnaire **preferred LA injections** to daily oral treatment

Guar. AIDS 2024. Abstr OAB2606LB.

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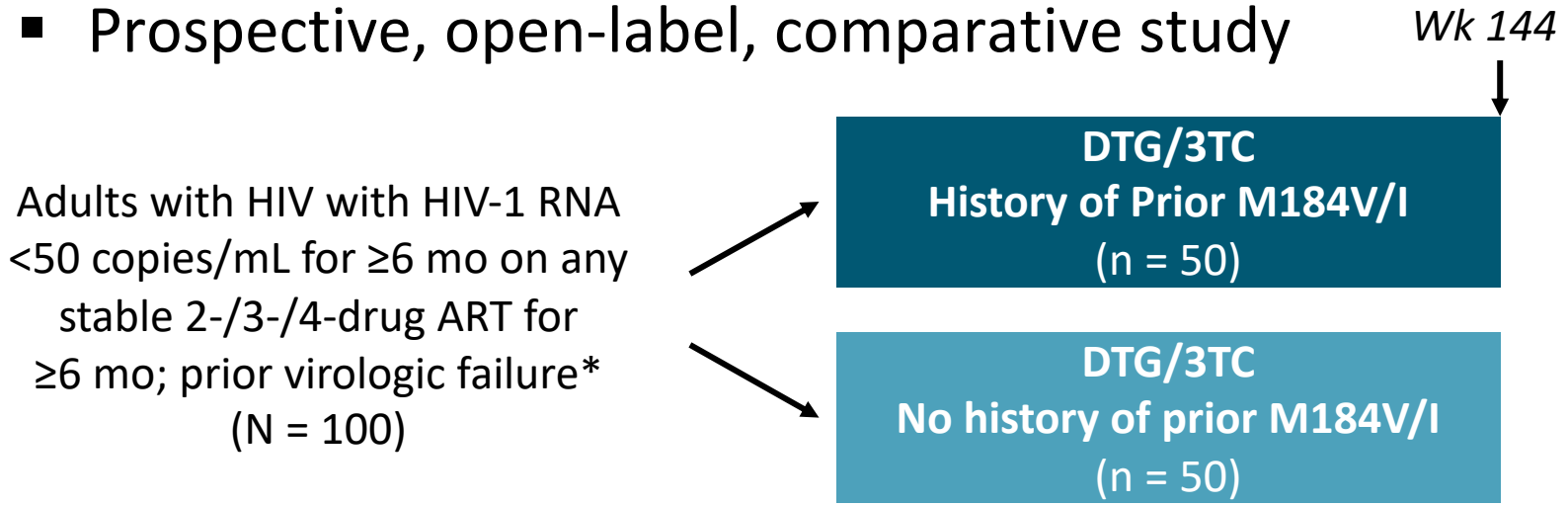
SOLAR-3D: Switching to DTG/3TC in Heavily Treatment–Experienced People Who Are Virologically Suppressed

- Prospective, open-label, comparative study



*≥2 prior ART with either: failure to attain HIV1-RNA <50 copies/mL, confirmed rebound >200 copies/mL, or documented genotypic/phenotypic resistance.

- **Primary endpoint:** proportion of participants with HIV-1 RNA ≥50 copies/mL at Wk 48 and 96 (FDA Snapshot, ITT-E, per protocol)
- **Secondary endpoints:** HIV-1 RNA <50 copies/mL at Wk 48 and 96 (FDA Snapshot, ITT-E, per protocol), discontinuations from CVF (HIV-1 RNA ≥50 copies/mL followed by HIV-1 RNA ≥200 copies/mL)

Baseline Characteristics:

- Participants with prior M184V/I had significantly greater:
  - Median age
  - Median time since HIV diagnosis
  - Median ART duration
  - Median prior ART regimens
  - Median duration of suppression

Blick. AIDS 2024. Abstr SS0403LB.

SOLAR-3D: Switch Characteristics

Characteristic	Prior M184V/I (n = 50)	No Prior M184V/I (n = 50)
On 3TC/FTC, n (%)	34 (68)	39 (78)
Median time on DTG/3TC, wk (IQR)	137.4 (133-151)	138.3 (132-151)
Median CD4 at switch		
▪ CD4% (IQR)	27 (24-37)	32 (27-39)
▪ Absolute count, cells/mm^3 (IQR)	617 (412-758)	593 (434-812)
▪ <200 cells/mm^3, n (%)	1 (2)	0
▪ <350 cells/mm^3, n (%)	7 (14)	3 (6)
Median HIV-1 RNA at switch		
▪ Copies/mL (IQR)	1 (1-19)	1 (1-19)
▪ Log_{10} (IQR)	0 (0-1.3)	0 (0-1.3)
▪ HIV-1 RNA >50 copies/mL, n (%)	1 (2)*	1 (2)†
▪ TND, n (%)	28 (56)	30 (60)

Historical GT vs Proviral DNA NGS, n (%)	Prior M184V/I (n = 50)	No Prior M184V/I (n = 50)
M184V/I on historical GT, n (%)	50 (100)	0
Proviral DNA by NGS, n(%)	41 (82)	29 958)
▪ M184V/I present	15 (37)	0
▪ M184V/I absent	26 (63)	29 (100)
▪ K65R present	1 92)	0
▪ K65R present with Q151M	0	1

*n = 1 participant with HIV-1 RNA <50 copies/mL at screening had HIV-1 RNA 73 copies/mL at baseline.

†n = 1 participant with HIV-1 RNA <50 copies/mL at screening had HIV-1 RNA 4150 copies/mL at baseline.

Blick. AIDS 2024. Abstr SS0403LB.

Slide credit: clinicaloptions.com

SOLAR-3D: Virologic Outcomes

ITT-E

	HIV-1 RNA ≥50 copies/mL, n (%)	Prior M184V/I (n = 50)	No Prior M184V/I (n = 50)
Primary Endpoint	Wk 48	1 (2)	3 (6)
	Wk 96	2 (4)	1 (2)
	Wk 144	2 (4)	3 (6)
	HIV-1 RNA <50 copies/mL, n (%)		
Secondary Endpoint	Wk 48	46 (92)	44 (88)
	Wk 96	42 (84)	44 (88)
	Wk 144	37 (74)	36 (72)

Per-Protocol

HIV-1 RNA ≥50 copies/mL, n/N (%)	Prior M184V/I (n = 50)	No Prior M184V/I (n = 50)
Wk 48	1/47 (2.1)	3/47 (6.4)
Wk 96	2/44 (4.6)	1/45 (2.2)
Wk 144	2/39 (5.1)	3/39 (7.7)
HIV-1 RNA <50 copies/mL, n/N (%)		
Wk 48	46/47 (97.9)	44/47 (93.6)
Wk 96	42/44 (95.5)	44/45 (97.8)
Wk 144	37/39 (94.9)	36/39 (92.3)

- No treatment-emergent resistance observed in either group and no participants discontinued treatment for CVF
- No new safety signals observed

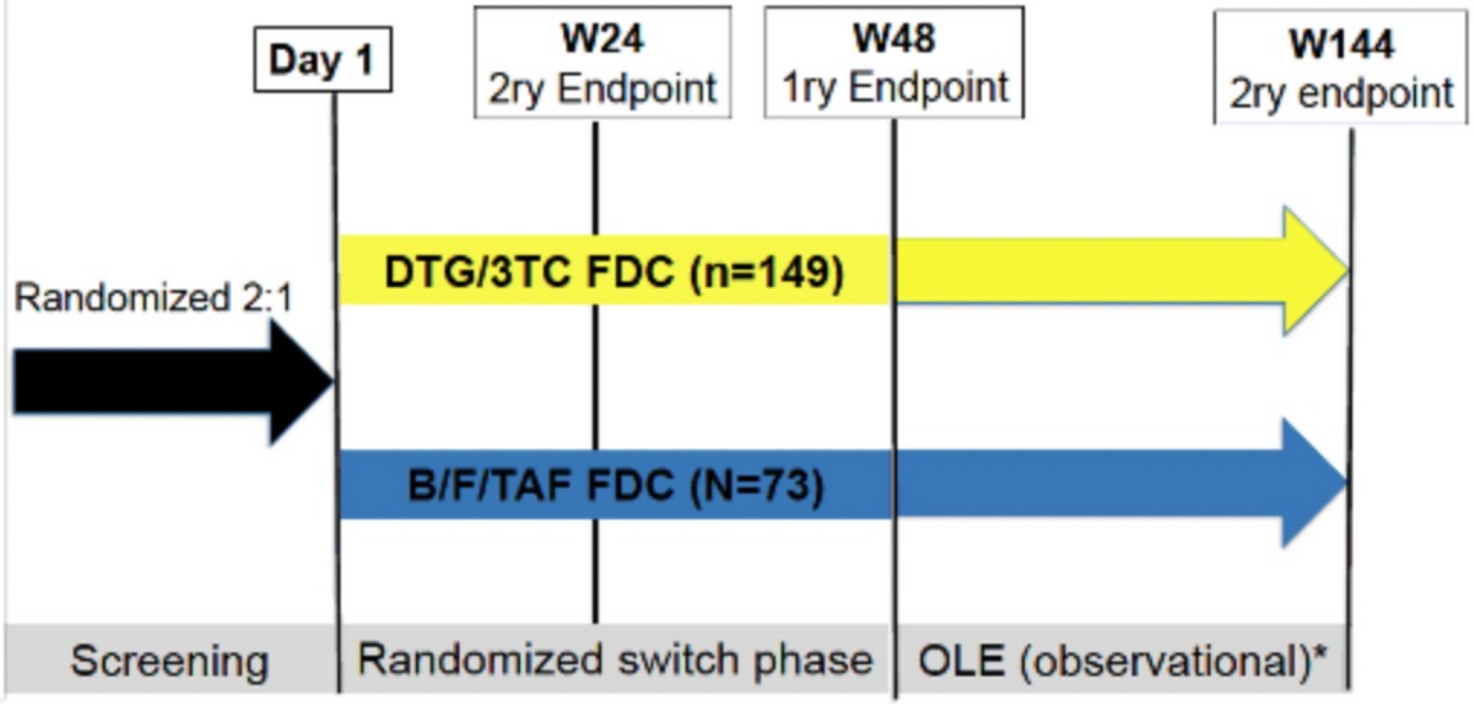
Blick. AIDS 2024. Abstr SS0403LB.

DYAD Study: Switching to DTG/3TC vs continuing BFTAF in virologically suppressed people with HIV

- Single center study (Orlando)
- Adds to TANGO and SALSA DTG/3TC switch studies by focusing on those on BFTAF

Eligibility criteria

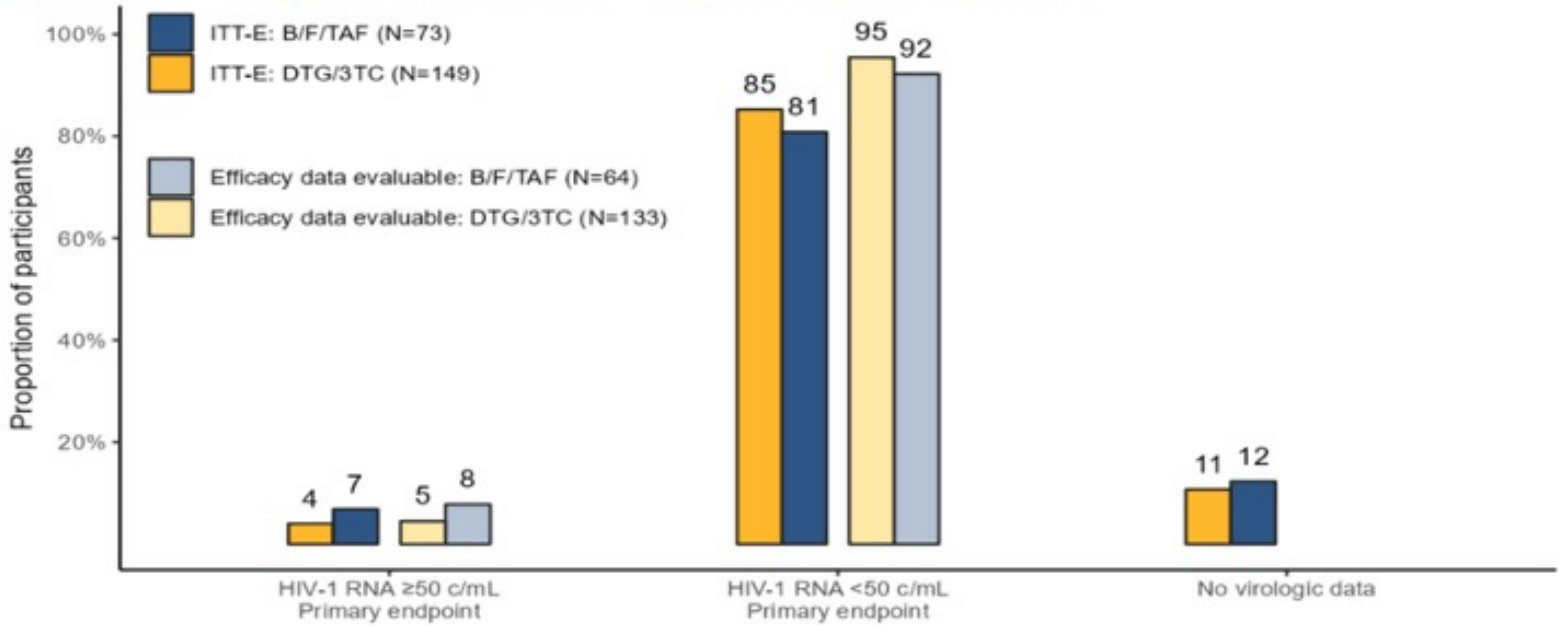
- On B/F/TAF for ≥3 months
- Two documented HIV-1 RNA measurements <50 copies/mL on B/F/TAF at least 3 months apart
- No HBV infection or acute need for HCV therapy
- No history of prior virologic failure (VF)
- No suspected or documented INSTI resistance
- History of 1-2 thymidine analogue mutations (TAMs), and other RT substitutions allowed, with the following exceptions: History of 3 or more TAMs (M41L, D67N, K70R, L210W, T215F/Y, and K219Q/E/N/R), M184V/I, T69-insertions, or K65R/E/N



*Open-label extension follows patients after they exit DYAD in the real-world and collects 96- and 144-week efficacy and safety data recorded in the EMR

DYAD Study: Switching to DTG/3TC vs continuing BFTAF in virologically suppressed people with HIV

Figure 1. Virologic outcomes at Week 48 by FDA Snapshot analysis



Abbreviations. B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; DTG, dolutegravir; 3TC, lamivudine

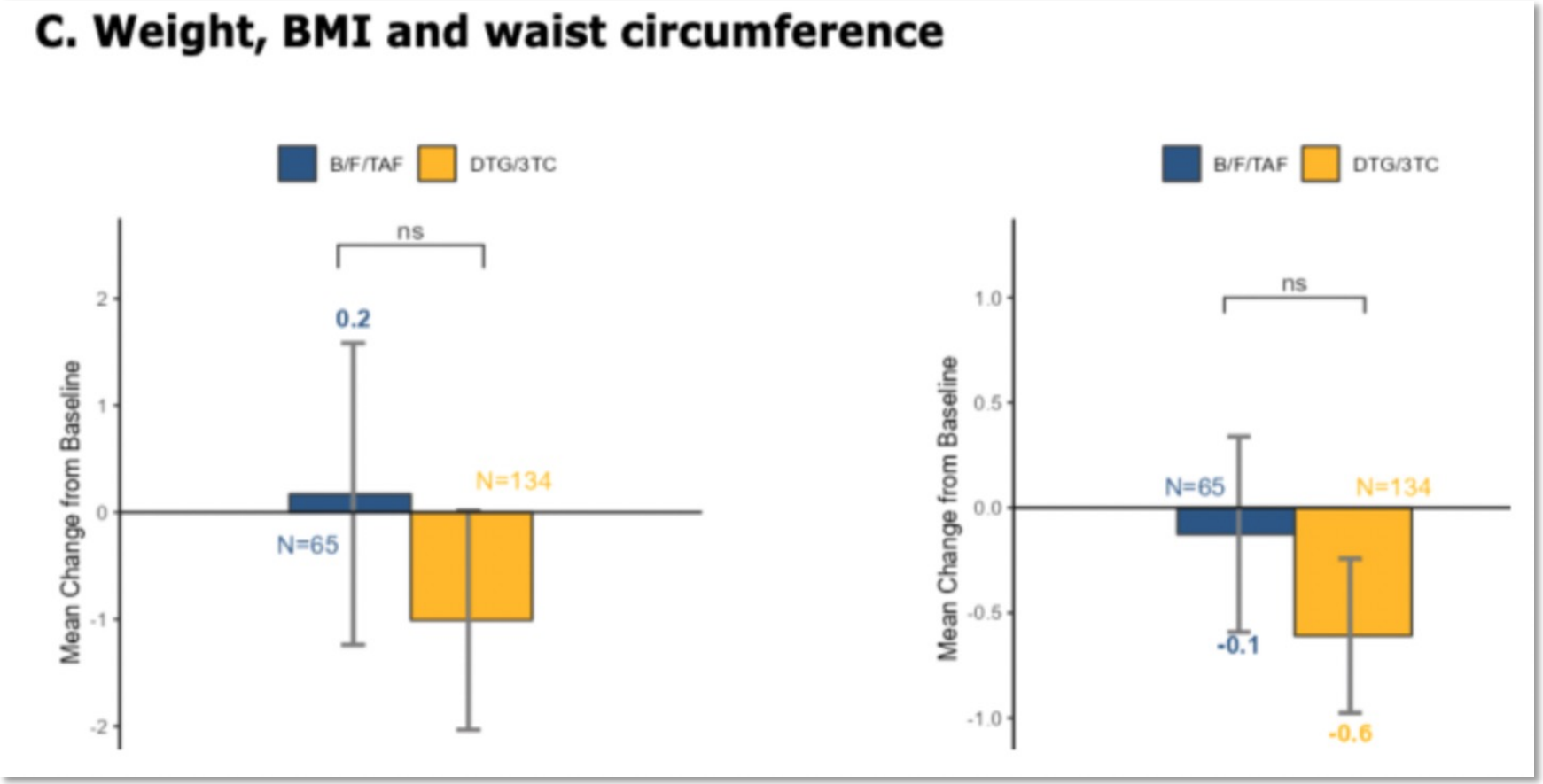
Table 2. Snapshot outcomes at Week 48

	DTG/3TC N=149	B/F/TAF N=73	Adjusted Treatment Difference (95% CI)
HIV-1 RNA≥50 c/mL	6 (4)	5 (7)	-2.8% (-11.4%, 3.1%)
HIV-1 RNA<50 c/mL	127 (85)	59 (81)	4.4% (-5.6%. 16.0%)
No virologic data	16 (11)	9 (12)	

Abbreviations. B, bictegravir; F, emtricitabine; TAF, tenofovir alafenamide; DTG, dolutegravir; 3TC, lamivudine; CI, confidence interval; c/ml, copies/mL

At Week 48, 6 (4%) participants on DTG/3TC and 5 (7%) on B/F/TAF had HIV-1 RNA≥50 c/mL (treatment difference -2.8%, 95% confidence interval [-11.4%, 3.1%]) meeting noninferiority criteria

DYAD Study: Switching to DTG/3TC vs continuing BFTAF in virologically suppressed people with HIV



- DTG/3TC did not lead to significant difference in change of lipids or creatinine. eGFR decline in DTG/3TC that was small but statistically significant.

PASO DOBLE: Switching to DTG/3TC vs BFTAF in virologically suppressed people with HIV

- Multicenter, randomized, open-label phase IV trial in Spain

Adults with HIV-1 RNA <50 c/mL for ≥24 wk; current ART with ≥1 pill/day including either COBI booster, EFV, or TDF; no earlier VF or ART resistance; no previous use of DTG or BIC; no chronic HBV
(N = 553)

Stratified by TAF use at baseline, sex at birth

Randomized 1:1

DTG/3TC
(n = 277)

BIC/FTC/TAF
(n = 276)

- Primary endpoint: plasma HIV-1 RNA ≥50 c/mL at Wk 48 by FDA Snapshot with noninferiority margin of 4%
- Key secondary endpoints: efficacy, safety, tolerability, weight change

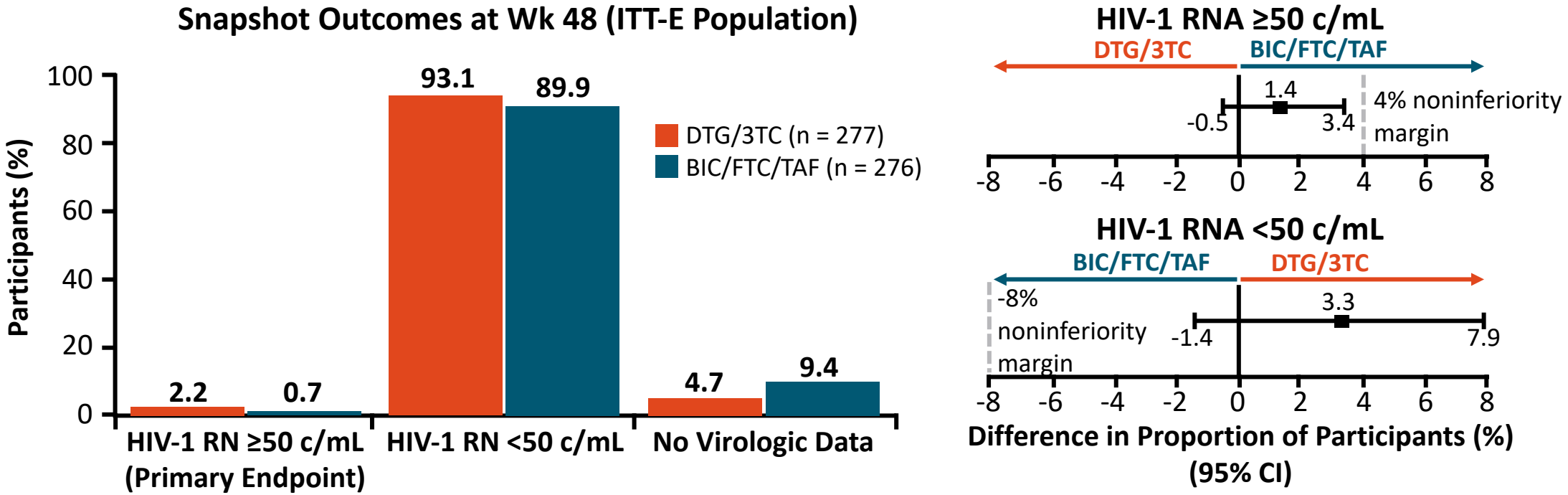
Martinez. AIDS 2024. Abstr OAB3606LB.

PASO-DOBLE: Baseline ART Regimens

Agent/Class, n (%)	DTG/3TC (n = 277)	BIC/FTC/TAF (n = 276)
NRTI 1		
▪ TAF	77 (27.8)	78 (28.3)
▪ ABC	59 (21.3)	52 (18.8)
▪ TDF	92 (33.2)	103 (37.3)
▪ No NRTI 1	49 (17.7)	43 (15.6)
NRTI 2		
▪ 3TC	70 (25.3)	64 (23.2%)
▪ FTC	182 (65.7)	190 (68.8%)
▪ None	25 (9.0)	22 (8.0%)
Core drug		
▪ NNRTI only	138 (49.8)	141 (51.1)
▪ INSTI only	44 (15.9)	49 (17.8)
▪ PI only	93 (33.6)	82 (29.7)
▪ >1 core drugs	2 (0.7)	4 (1.4)

Martinez. AIDS 2024. Abstr OAB3606LB.

PASO-DOBLE: Virologic Efficacy



- By Wk 48, ≥1 virologic blip in 5.8% (16/277) receiving DTG/3TC and in 9.4% (26/276) receiving BIC/FTC/TAF; *P* = .106
  - Through Wk 48, 98 vs 152 total blips in those receiving DTG/3TC and BIC/FTC/TAF, respectively
- Confirmed virologic failure through Wk 48 in 1 participant receiving BIC/FTC/TAF vs 0 in those receiving DTG/3TC; no cases of emergent resistance in either arm

Martinez. AIDS 2024. Abstr OAB3606LB.

Slide credit: clinicaloptions.com

PASO-DOBLE: Body Weight Outcomes at Wk 48

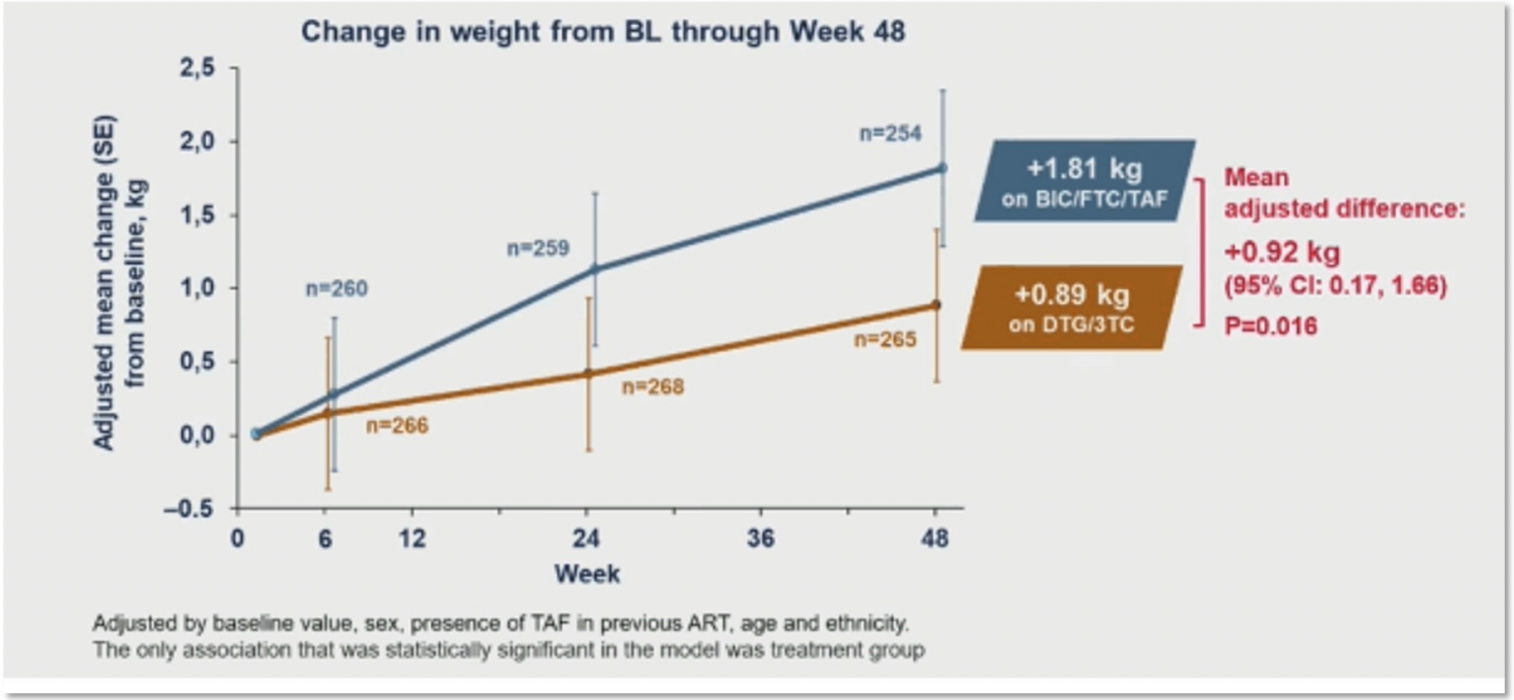
Outcome at Wk 48	DTG/3TC (n = 265)	BIC/FTC/TAF (n = 254)	Mean Adjusted Difference or OR (95% CI)
Weight change from baseline, kg	+0.89	+1.81	+0.92 (0.17-1.66)
BMI change from baseline, kg/m^2	+0.32	+0.64	+0.32 (0.06-0.58)
Percent of participants with weight gain >5% *Adjusted OR	20.0	29.9	1.81* (1.19-2.76) *P* = .006

- Prior use of ABC or TDF predisposed to **greater weight gain** with **BIC/FTC/TAF** than **DTG/3TC (less weight gain)**

Martinez. AIDS 2024. Abstr OAB3606LB.

Slide credit: clinicaloptions.com

PASO DOBLE: Switching to DTG/3TC vs BFTAF in virologically suppressed people with HIV

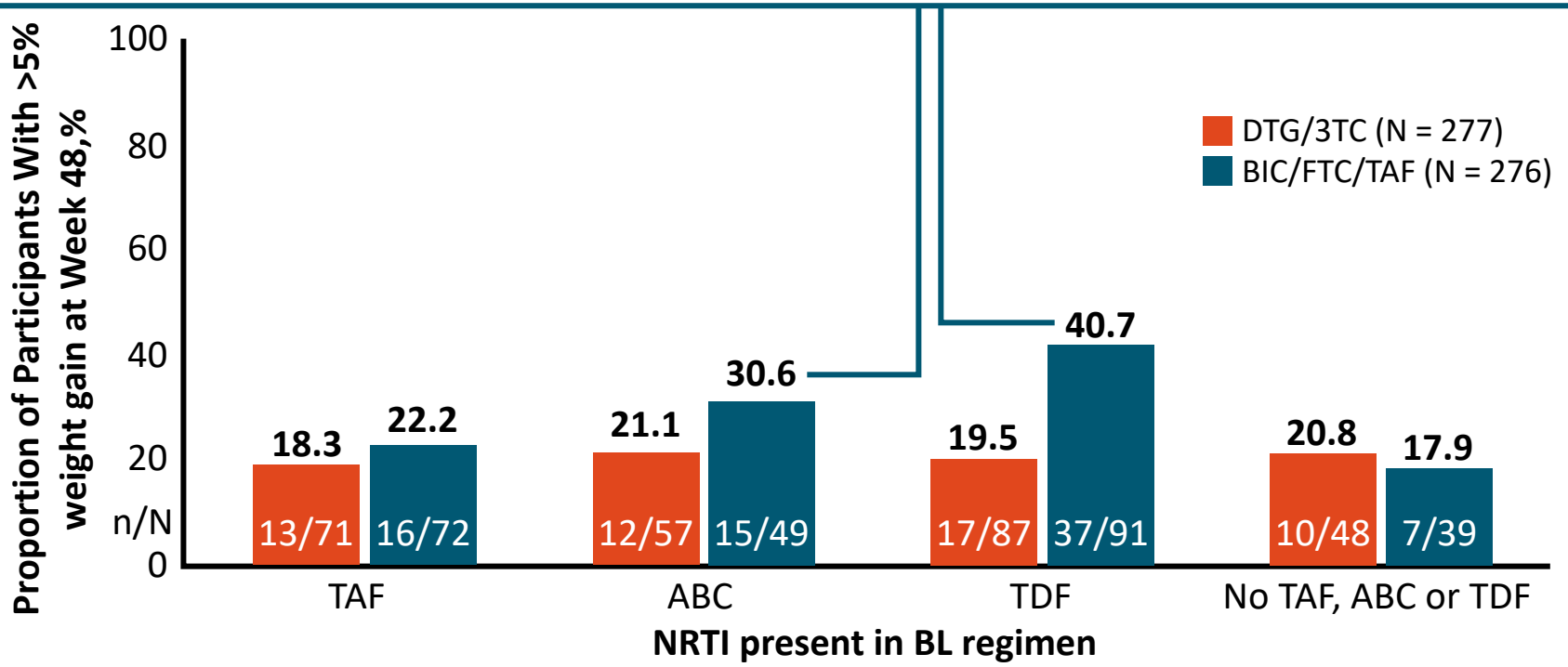


Martinez. AIDS 2024. Abstr OAB3606LB.

Slide credit: clinicaloptions.com

PASO-DOBLE: Body Weight Outcomes by Baseline NRTI

- Change in weight with BIC/TAF/FTC may depend on NRTI of previous regimen
  - In **DTG/3TC** arm, proportion with >5% weight gain was similar regardless of BL NRTI
  - In **BIC/FTC/TAF** arm, proportion with >5% weight gain was highest after switch from TDF or ABC

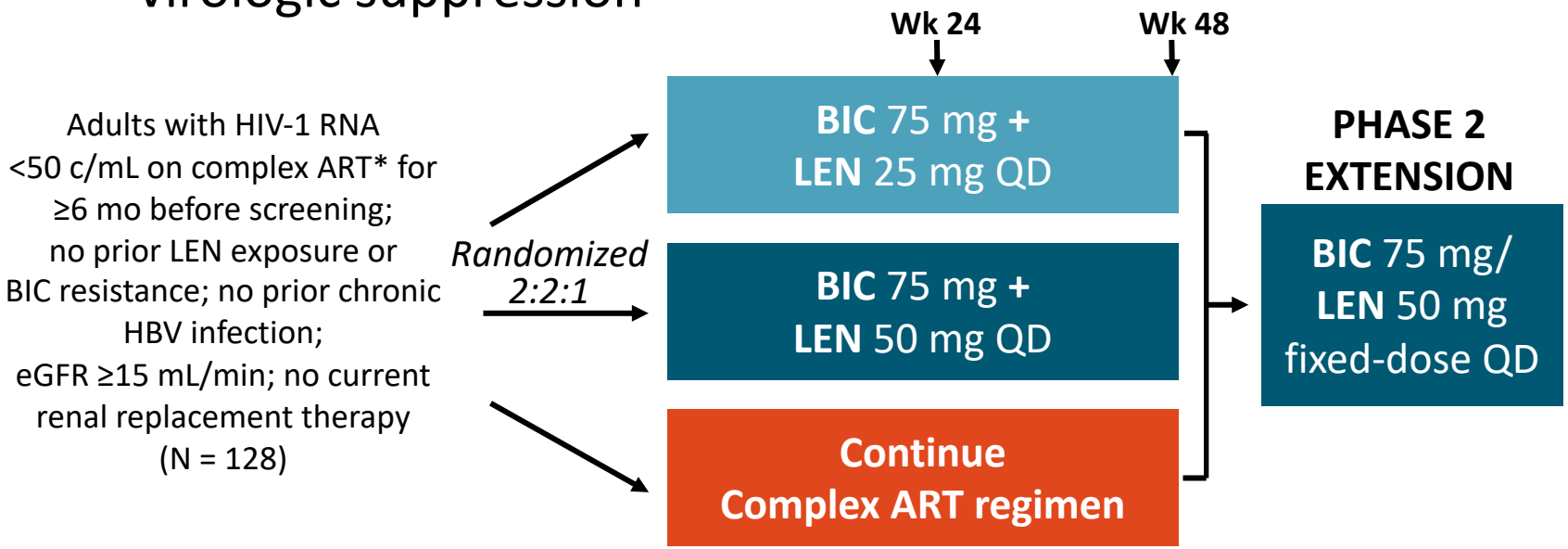


Martinez. AIDS 2024. Abstr OAB3606LB.

Slide credit: clinicaloptions.com

ARTISTRY-1: Switch to Oral BIC + LEN in People With Virologically Suppressed HIV on Complex ART

- Multicenter, randomized, open-label phase II/III study
- In primary 24-wk analysis, BIC + LEN effectively maintained virologic suppression[1]



- **Wk 48 endpoints**: proportion with HIV-1 RNA <50 c/mL (FDA Snapshot), CD4+ count change from baseline, AEs[2]

Complex ART at baseline:

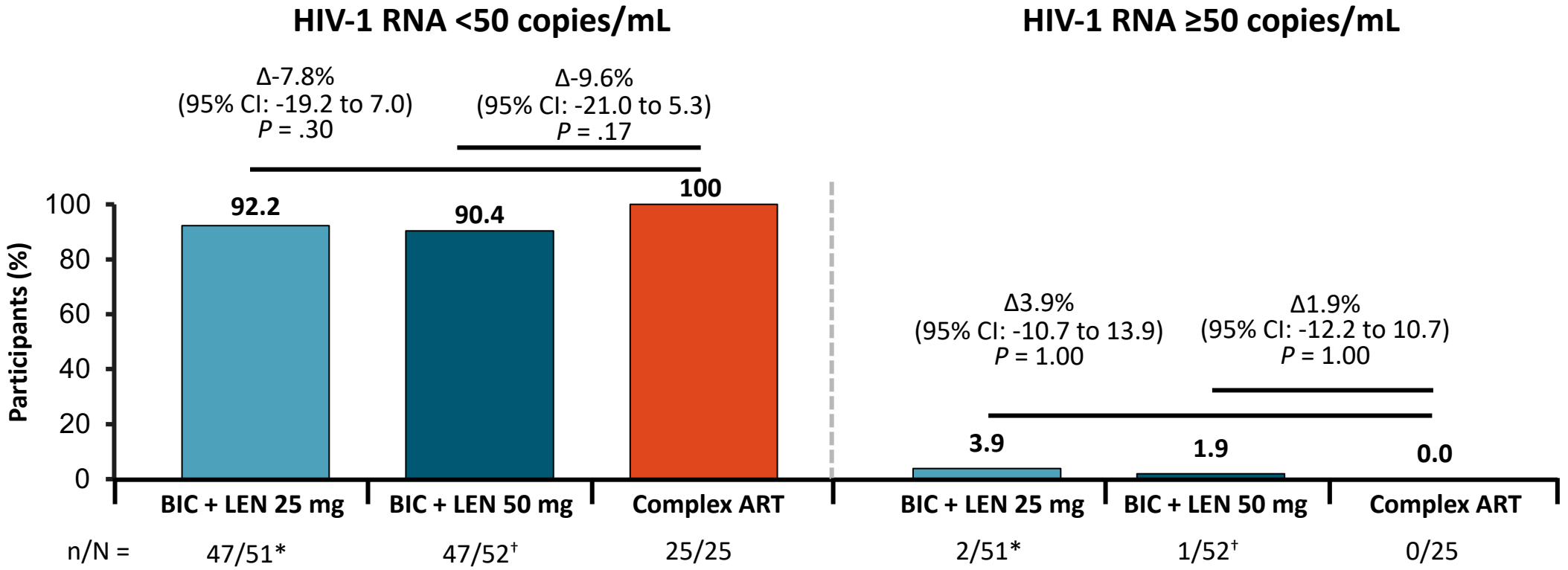
- 41.4% taking ART dosed 2x/day
- Pills/day: 2 (43.0%), 3 (18.8%), 4 (10.9%), ≥5 (27.3%)
- 72% on a PI; among those, 66% received a PI + INSTI

Baseline Characteristics:

- Median age, yr: 60 (26-79)
- Male at birth, n (%): 104 (81.2)
- White, n (%): 83 (64.8)

1. Mounzer. CROI 2024. Abstr 642. 2. Mounzer. AIDS 2024. Abstr OAB2602.

ARTISTRY-1: Virologic Suppression at Wk 48 With Switch to Oral BIC + LEN

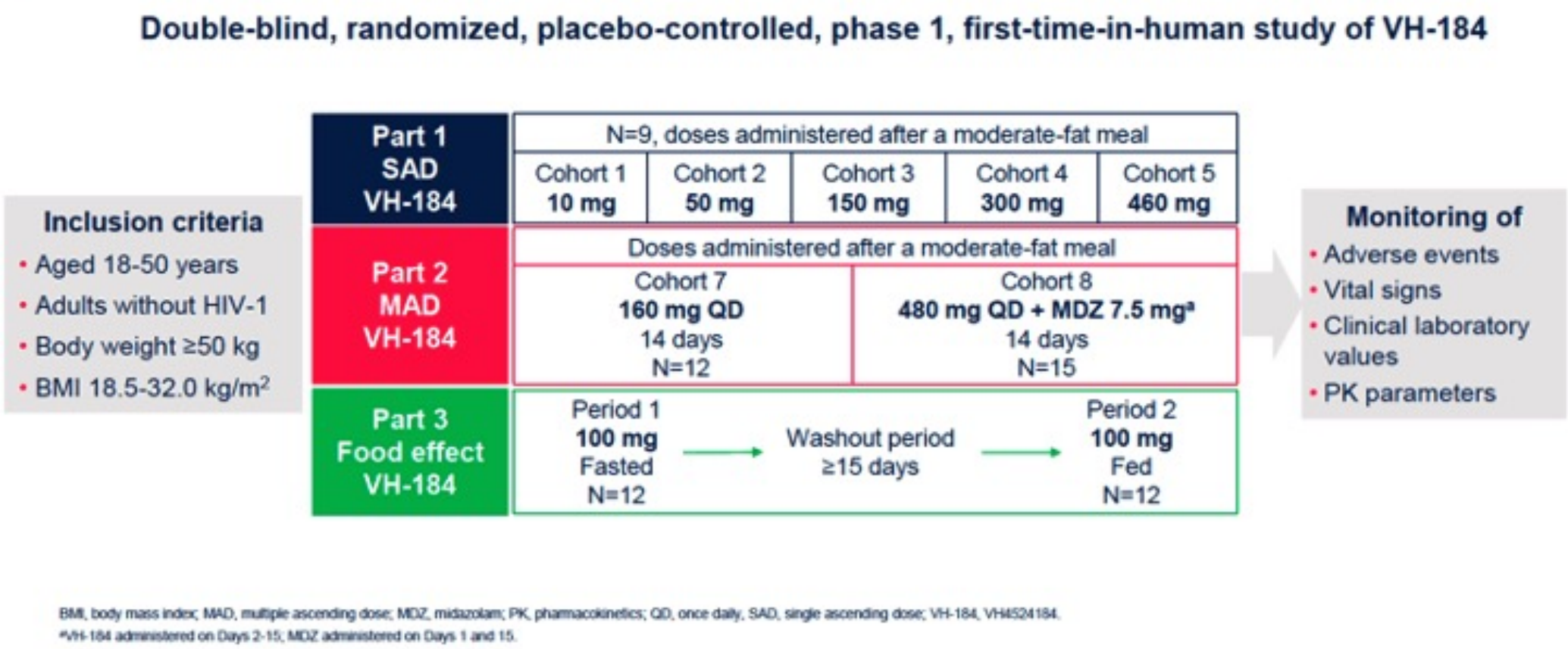


*No virologic data in Wk 48 window: n = 2. †No virologic data in Wk 48 window: n = 4.

- Changes in CD4+ cell count and percentage were comparable among treatment groups

VH184 – 3rd generation INSTI: Phase 1 trial

- VH4524184 (VH-184) is a third-generation INSTI with long-acting potential in development for HIV-1 treatment
- In vitro, VH-184 active against DTG and CAB resistant viruses



Rogg. AIDS 2024..

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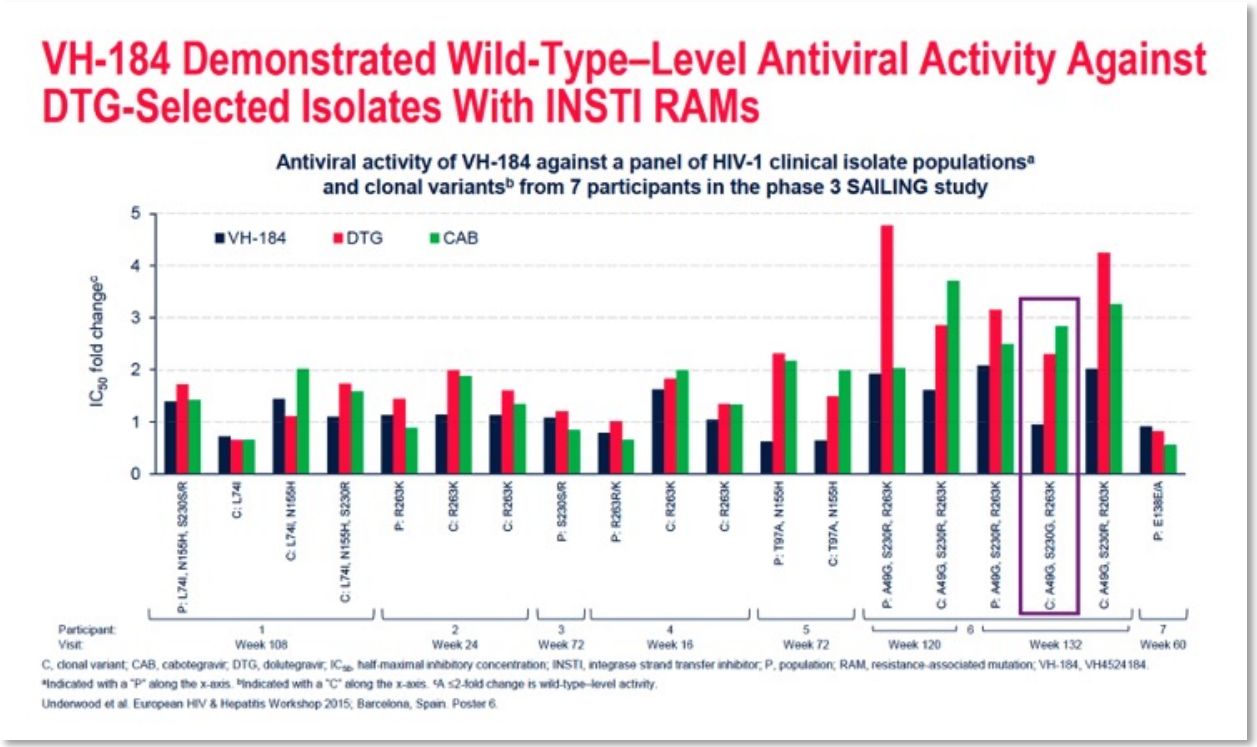
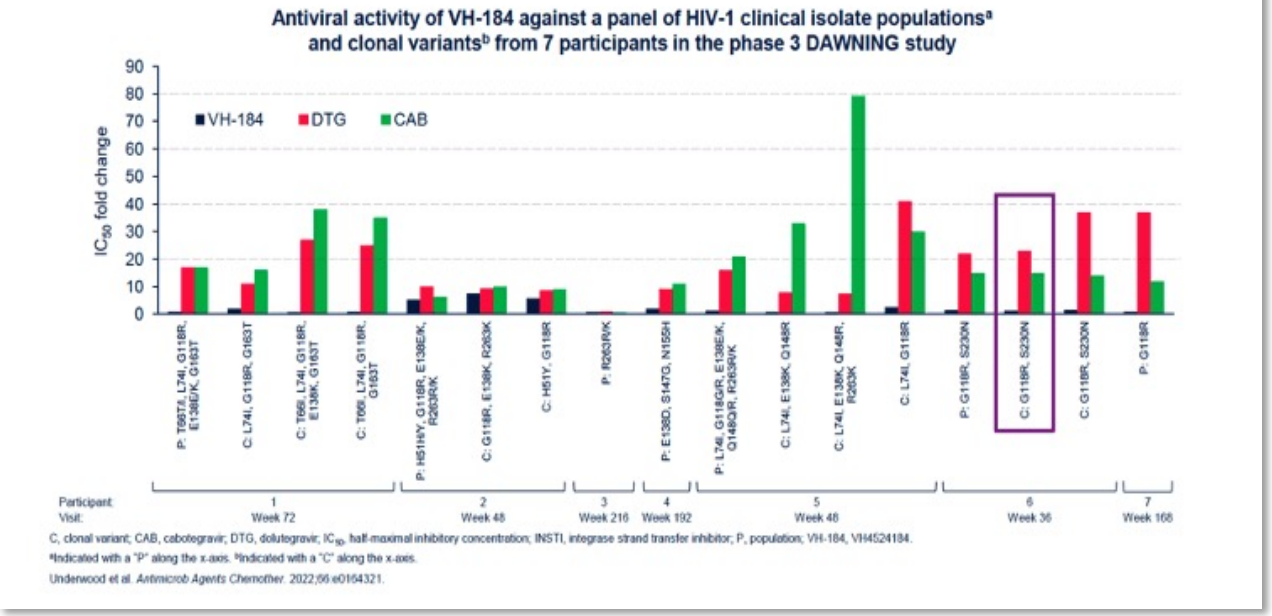
VH-184 Demonstrated Wild-Type–Level Antiviral Activity Against DTG-Selected Isolates With INSTI RAMs



C, clonal variant; CAB, cabotegravir; DTG, dolutegravir; IC_{50}, half-maximal inhibitory concentration; INSTI, integrase strand transfer inhibitor; P, population; RAM, resistance-associated mutation; VH-184, VH4524184.
[a]Indicated with a "P" along the x-axis. [b]Indicated with a "C" along the x-axis. [c]A ≤2-fold change is wild-type–level activity.
Underwood et al. European HIV & Hepatitis Workshop 2015; Barcelona, Spain. Poster 6.

VH-184 Demonstrated Potent Antiviral Activity Against DTG-Selected INSTI-Resistant Isolates



C, clonal variant; CAB, cabotegravir; DTG, dolutegravir; IC_{50}, half-maximal inhibitory concentration; INSTI, integrase strand transfer inhibitor; P, population; VH-184, VH4524184.
[a]Indicated with a "P" along the x-axis. [b]Indicated with a "C" along the x-axis.
Underwood et al. *Antimicrob Agents Chemother.* 2022;66:e0164321.

Rogg. AIDS 2024..

Why does this matter? HIV Treatment

- Real-er world data demonstrate experience with CAB/RPV outside of clinical trials to be generally goof among those desiring injectable therapy.
- More data support use of DTG/3TC in people with virus harboring 184V but studies have been small.
- Switching to DTG/3TC from BFTAF maintains viral suppression without major changes to metabolic parameters. DYAD and PASO DOBLE suggest possible weight difference between DTG/3TC and BFTAF following switch, especially from TDF or ABC.
- Oral LEN+BIC may be a simple option for people on complex regimens.
- VH-184 among new ART that can be long acting and be active against virus resistant to current therapies.

HIV Complications

REPRIEVE: Risk of Cardiovascular Events With ABC in People With HIV

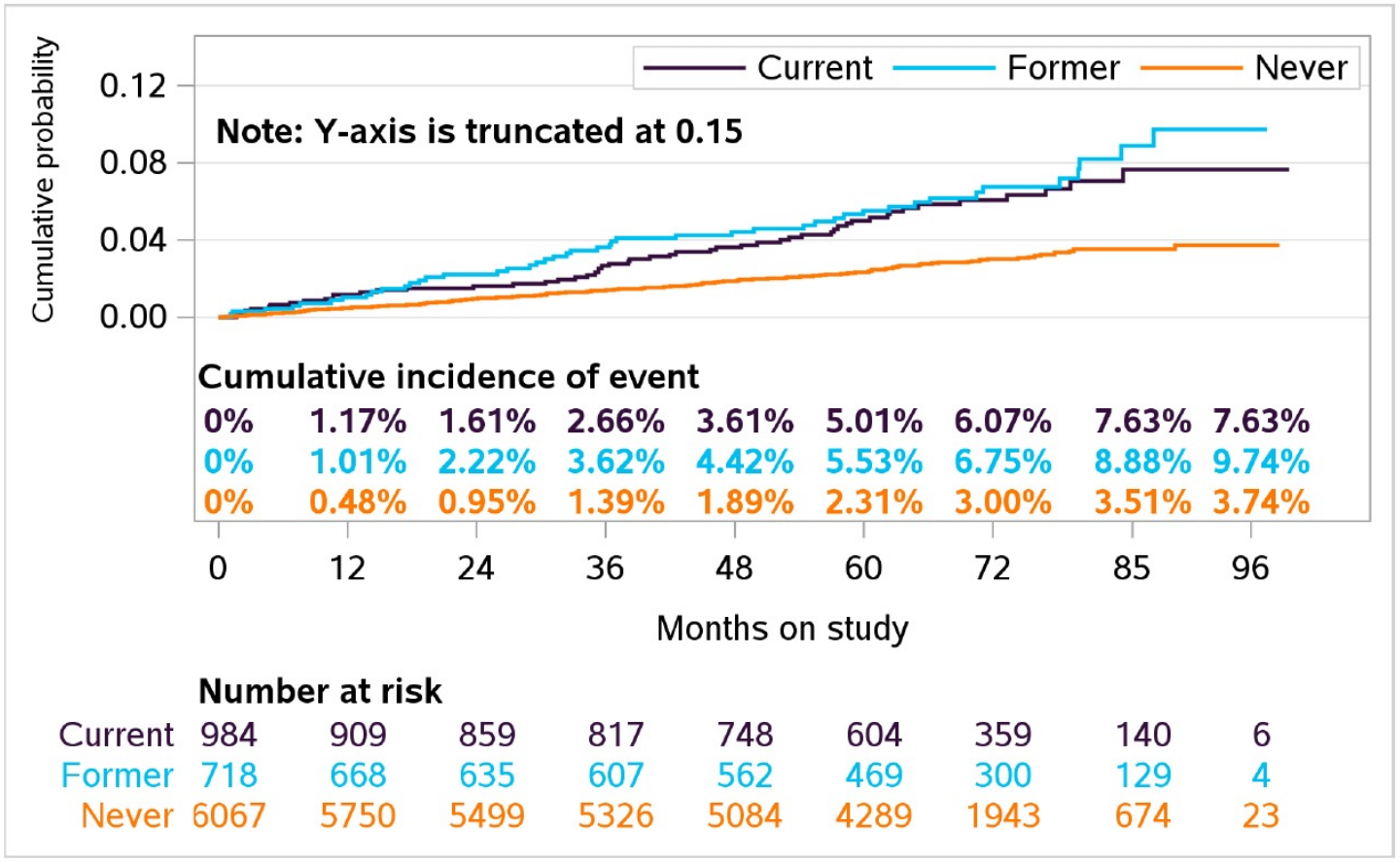
- Multicenter, randomized, double-blind study of people with HIV (N = 7769) enrolled 2015-2019 with follow-up through July 2023
  - On stable ART for ≥180 days
  - CD4+ cell count >100 c/mm^3
  - Age 40-75 yr
  - At low to moderate risk of CVD
- Study demonstrated 36% reduction in MACE (including MI, TIA/stroke, PAD, revascularization, CV death) with pitavastatin vs placebo

- **Current analysis** in ITT population assessed effect of exposure to **ABC** on first MACE, median follow-up of 5.6 yr
- 22% had history of ABC exposure (n = 1702)
  - 9% former use (median 3.0 yr)
  - 13% use at randomization (median 1.47 yr)
- Median ASCVD risk score (Q1, Q3):
  - Prior ABC exposure 5.40 (3.10, 7.80)
  - No ABC exposure 4.20 (1.90. 6.80)
  - Total population 4.50 (2.10, 7.00)

Fichtenbaum. AIDS 2024. Abstr OAB3406LB. Grinspoon. NEJM. 2023;389:687. Grinspoon. NEJM. 2024;390(17):1626.

REPRIEVE: Risk of Major Cardiovascular Events (MACE) With ABC in People With HIV

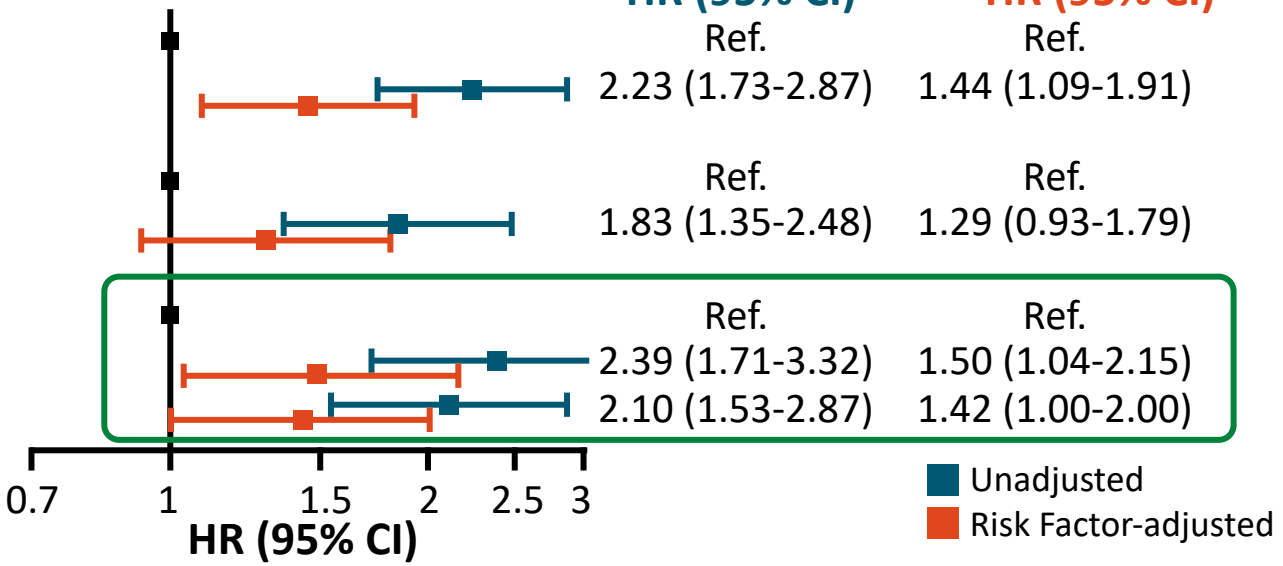
Cumulative Incidence of MACE with Abacavir



Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

REPRIEVE: Major Cardiovascular Events

	Events	Participants	Unadjusted HR (95% CI)	Risk Factor-Adjusted HR (95% CI)
History of ABC exposure				
No	161	6092	Ref.	Ref.
Yes	96	1677	2.23 (1.73-2.87)	1.44 (1.09-1.91)
ABC use at randomization				
No	205	6785	Ref.	Ref.
Yes	52	984	1.83 (1.35-2.48)	1.29 (0.93-1.79)
ABC exposure				
Never	160	6067	Ref.	Ref.
Former	45	718	2.39 (1.71-3.32)	1.50 (1.04-2.15)
Current	52	984	2.10 (1.53-2.87)	1.42 (1.00-2.00)



- Current and former use of **ABC** was associated with a **~42%-50% higher risk of subsequent MACE**
  - ABC effect on MACE was *not* changed by exposure to INSTIs, NNRTIs, or PIs
- Current and former use of TDF, PIs, and thymidine analogs were *not* associated with subsequent MACE

Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

Slide credit: clinicaloptions.com

AFRICOS: Incident Hypertension and DTG-Based ART

- Prospective cohort analysis of incidence of HTN in people with HIV receiving ART (anchor drug: DTG, EFV, NVP, or PI/RTV) and people without HIV in Kenya, Nigeria, Tanzania, and Uganda
  - Exclusion criteria: HTN, people without HIV who seroconverted, pregnancy
  - Follow-up every 6 mo after enrollment visit
- Incident HTN: persistently elevated BP (SBP ≥140 mm Hg and/or DBP ≥90 mm Hg) at ≥2 consecutive study visits, or receipt of BP-lowering medication
- Current analysis assessed **association between DTG and incident HTN** in N = 3250 people with ≥2 study visits

Romo. AIDS 2024. Abstr OAB3404.

AFRICOS: Study Population and Incident Hypertension

Baseline Characteristic	Study Population (N = 3250)
HIV status, n (%)	
▪ With HIV	2705 (84.4)
▪ Without HIV	545 (16.8)
Sex, n (%)	
▪ Male	1370 (42.2)
▪ Female	1880 (57.8)
Mean age at enrollment, yr (SD)	36 (12)
Study site, n (%)	
▪ Kayunga, Uganda	575 (17.7)
▪ South Rift Valley, Kenya	1142 (35.1)
▪ Kisumu, Kenya	641 (19.7)
▪ Mbeya, Tanzania	555 (17.1)
▪ Abuja and Lagos, Nigeria	337 (10.4)

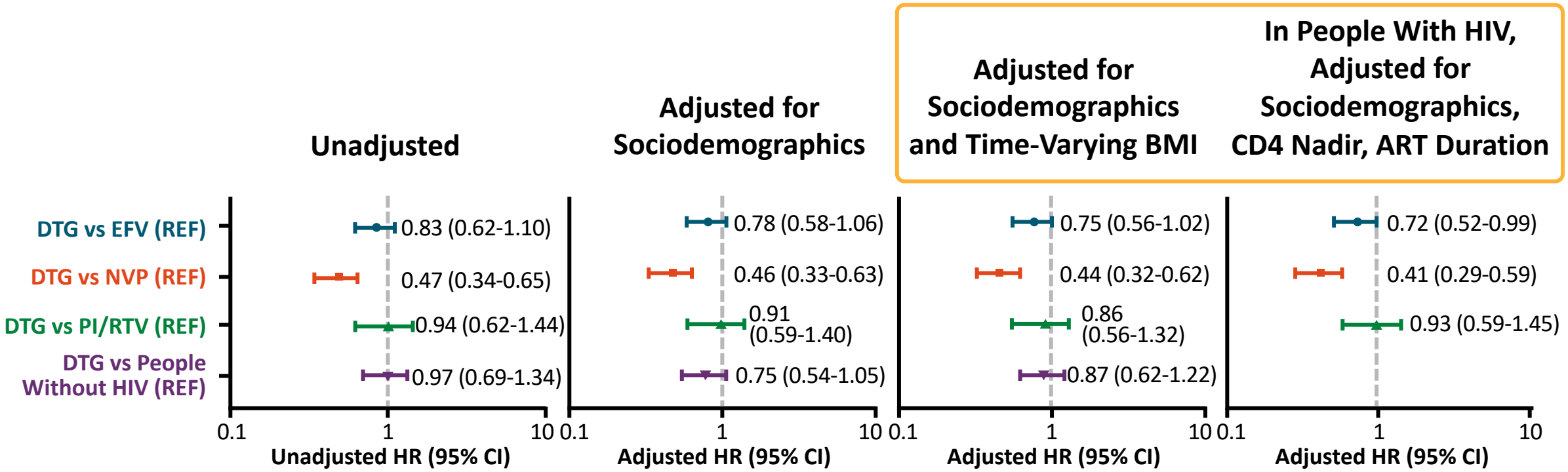
Study group	Incident HTN, n (%)	Median Follow-up, Yr (IQR)
People with HIV with ART anchor exposure		
▪ **DTG**	**1907 (70.5)**	**3.4 (2.2-4.0)**
▪ EFV	1737 (64.2)	4.2 (3.0-5.5)
▪ NVP	615 (22.7)	4.5 (3.5-5.4)
▪ PI/RTV	310 (11.5)	6.0 (3.7-7.9)
People without HIV	545 (100)	7.5 (5.2-8.7)

- 427 (13.1%) of participants had incident HTN during study follow-up

Romo. AIDS 2024. Abstr OAB3404.

Slide credit: clinicaloptions.com

AFRICOS: Incident Hypertension Across Anchor ART Groups and in People Without HIV



- DTG was **not** associated with significantly increased risk of HTN compared with EFV, NVP, or PI/RTV use or compared with people without HIV
- DTG was associated with significantly lower hazards of HTN compared with NVP

Romo. AIDS 2024. Abstr OAB3404.

Slide credit: clinicaloptions.com

Anal Cancer Screening Effectiveness

- Five different anal cancer screening strategies are listed in guidelines
- Effectiveness of screening approaches assessed among 1,620 PWH at Mt Sinai who underwent anal cytology, hrHPV testing, and high-resolution anoscopy. Anal HSIL rate = 42%

1. **Cytology alone**
2. **Cytology with hrHPV testing triage of >ASCUS**
3. **hrHPV testing alone**
4. **hrHPV testing with cytology triage of hrHPV positive**
5. **Cytology and hrHPV co-testing**

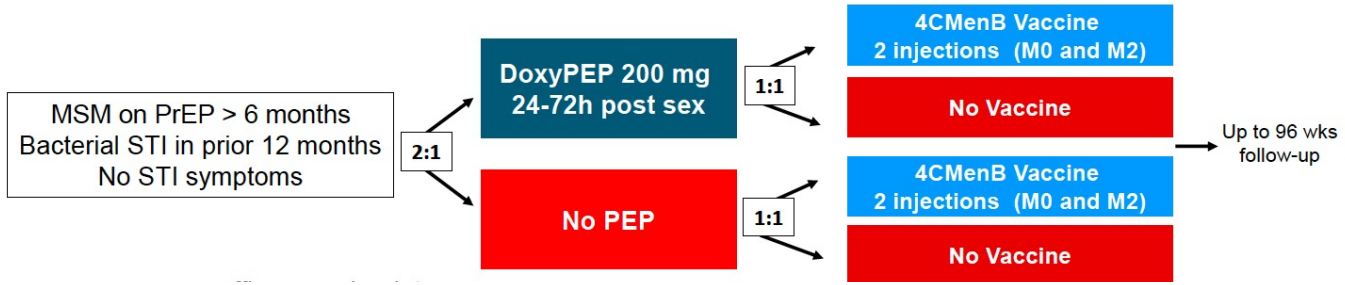
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	HRAs (%)
Cytology alone	88	30	48	77	77
Cytology + hrHPV testing triage of >ASCUS	85	47	54	81	67
hrHPV testing alone	96	27	49	92	83
hrHPV testing + cytology triage of hrHPV positive	85	48	54	81	66
Cytology + hrHPV co-testing	89	40	52	83	72

- All strategies showed comparable performance metrics.
- hrHPV testing alone had highest sensitivity and NPV but triggered the most diagnostic procedures
- hrHPV with cytology triage showed the highest specificity

Gaisa M, et al. AIDS2024. Abstract OAB0102.

DoxyVac Trial

- Multicenter, 2 x 2 factorial randomized, open-label, superiority, phase III trial (NCT04597424)



Screening for bacterial STI every 3 months
Dramatic reduction in bacterial STIs incidence

	Syphilis	Chlamydia	Gonorrhea
Relative risk reduction of STIs incidence (DoxyPEP arm *vs* noPEP arm)	79%	86%	33%

Molina *et al*, Lancet Inf Dis, 2024 May 23:S1473-3099(24)00236-6.

Conclusions

AIDS 2024

All GC isolates were resistant to tetracycline but the rate of high-level resistance was higher in the DoxyPEP arm.

There was no impact of DoxyPEP on ceftriaxone, ciprofloxacin and azithromycin susceptibility.

We identified a new GC cluster with Decreased Susceptibility to cefixime and HLR to tetracycline without clear association with doxyPEP.

SUPERBUG

Monitoring the emergence of 3rd generation cephalosporin resistant isolates remains critical.

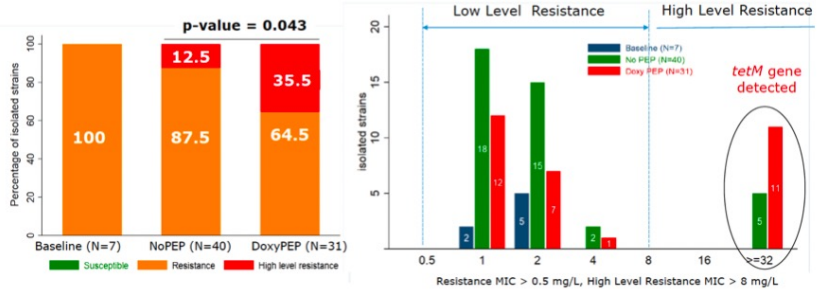
22 – 26 July · Munich, Germany and virtual aids2024.org

Bercot B, et al. AIDS 2024. Abstract SS0404LB.

Resistance to tetracycline, MIC distribution

78 GC isolates

More high-level tetracycline-resistant isolates in the DoxyPEP arm

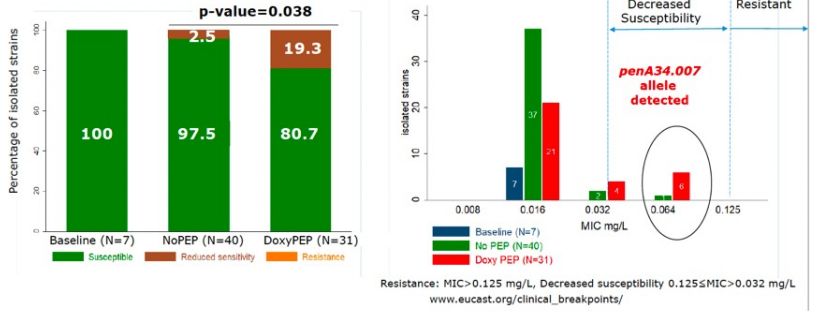


Molina *et al*, Lancet Inf Dis, 2024 May 23:S1473-3099(24)00236-6.; www.eucast.org/clinical breakpoints/

Decreased susceptibility to cefixime, MIC distribution

78 GC isolates

Isolates with Decreased Susceptibility to cefixime were more frequent in the doxyPEP arm.



Multimorbidity among ageing PWH in US South

- Descriptive analysis of multi-morbidities (2 or more) among PWH age 65+ in care at UNC in 2022-2023

Table 1. **Characteristics of PWH by Gender**

Characteristics	Female (n=89)	Male (n=210)	Overall (n=299)
Age (years)			
median (25th, 75th, max)	71.0 (68.0, 74.0, 90.0)	70.0 (67.0, 73.0, 90.0)	70.0 (67.0, 73.0, 90.0)
Race			
African American	68 (76.4)	99 (47.1)	167 (55.9)
White	16 (18.0)	97 (46.2)	113 (37.8)
Other	5 (5.6)	14 (6.7)	19 (6.4)
Years since HIV diagnosis			
median (25th, 75th, max)	25.0 (19.0, 29.0, 38.0)	25.0 (17.0, 31.0, 42.0)	25.0 (18.0, 30.0, 42.0)
Suppressed at last visit (<50)			
Yes	85 (95.5)	199 (94.8)	284 (95.0)
No	4 (4.5)	11 (5.2)	15 (5.0)
Ever on an integrase inhibitor in 2022-2023			
Yes	75 (84.3)	153 (73.6)	228 (76.8)
No	14 (15.7)	55 (26.4)	69 (23.2)
Visits to HIV clinic in 2022-2023			
<5 visits	45 (50.6)	89 (42.4)	134 (44.8)
5 or more visits	44 (49.4)	121 (57.6)	165 (55.2)
median (25th, 75th, max)	4 (3, 6, 24)	5 (4, 7, 24)	5 (3, 6, 24)

Comorbidity definitions:

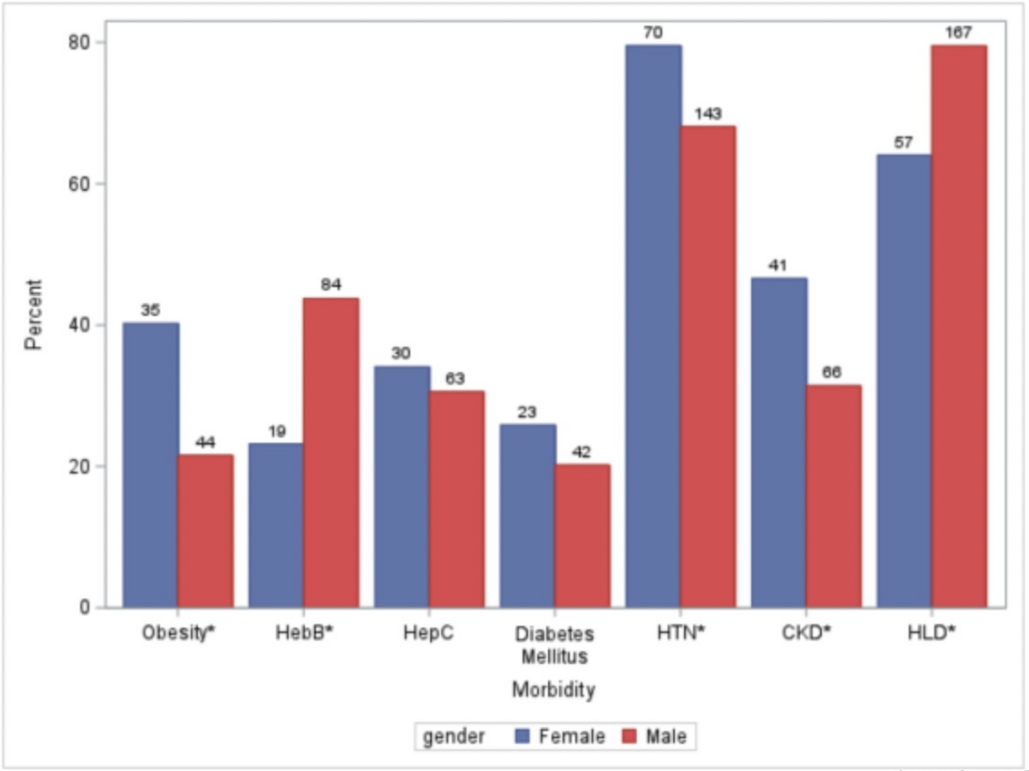
1. Diabetes Mellitus (DM): on a medication AND (a) ICD9/10 code OR (b) A1c ≥ 6.5
2. Hypertension (HTN): on a medication AND (a) ICD 9/10 code OR (b) elevated Blood Pressure
3. Chronic Kidney Disease (CKD): Stage 3 or greater in prior two visits (eGFR<60 computed using the 2021 CKD Epidemiology Collaboration equation)
4. Hyperlipidemia (HLD): antilipemic medication use
5. Hepatitis B: positive surface antigen, or core antibody, or DNA
6. Hepatitis C: positive antibody or RNA
7. Obesity: BMI ≥ 30kg/m^2

Menezes.. AIDS 2024..

Multimorbidity among ageing PWH in US South

- Descriptive analysis of multi-morbidities (2 or more) among PWH age 65+ in care at UNC in 2022-2023

Figure 1. **Prevalence of Comorbidities by Gender**



* p-value < 0.05

- Prevalence of multimorbidity (≥2 comorbidities) among older PWH was high (83.6%) but did not differ significantly by gender
- In multivariable analysis, duration (years) of HIV diagnosis was a statistically significant independent predictor of multimorbidity status after adjusting for age, race, gender, nadir CD4 cell count and ≥ 5 HIV clinic visits (p=0.0258)

Menezes.. AIDS 2024..

Why does this matter? Complications

- Further evidence of an association between abacavir and CVD.
- Further evidence that INSTI do not cause HTN
- Anal cancer screening with hrHPV and cytology has best performance
- DOXYPEP is important intervention to reduce STI among MSM. Drug resistance may limit its usefulness for gonorrhea.
- Further data demonstrate multi-morbidity prevalence among older PWH.

COVID-19

COVID-19: August 2024 Status

- COVID-19 continues to spread and be a major cause of death in the US (CDC)

Number of deaths for leading causes of death

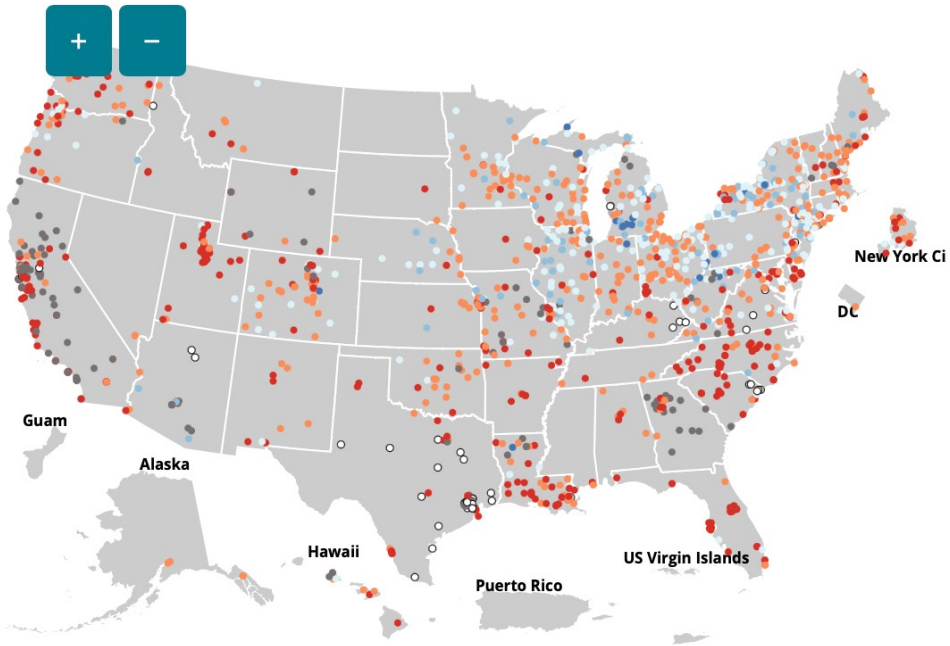
- Heart disease: 702,880
- Cancer: 608,371
- Accidents (unintentional injuries): 227,039
- COVID-19: 186,552
- Stroke (cerebrovascular diseases): 165,393
- Chronic lower respiratory diseases: 147,382
- Alzheimer's disease: 120,122
- Diabetes: 101,209
- Nephritis, nephrotic syndrome, and nephrosis: 57,937
- Chronic liver disease and cirrhosis: 54,803

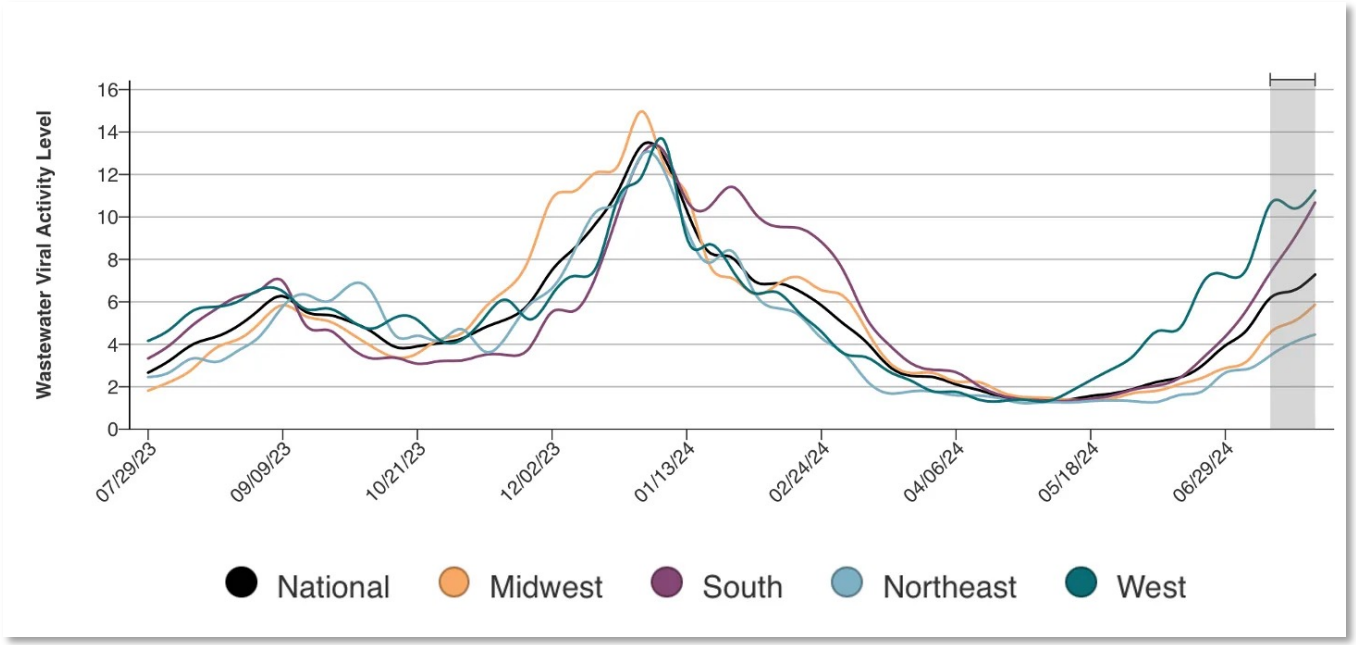
TOTAL DEATHS

1,197,470

COVID-19: August 2024 Status

- Tallying how many people getting infected with COVID-19 is hard given home testing and fewer reporting requirements than earlier in the pandemic.
- Wastewater is analyzed for SARS-CoV-2 levels and can serve as a proxy for burden of COVID-19

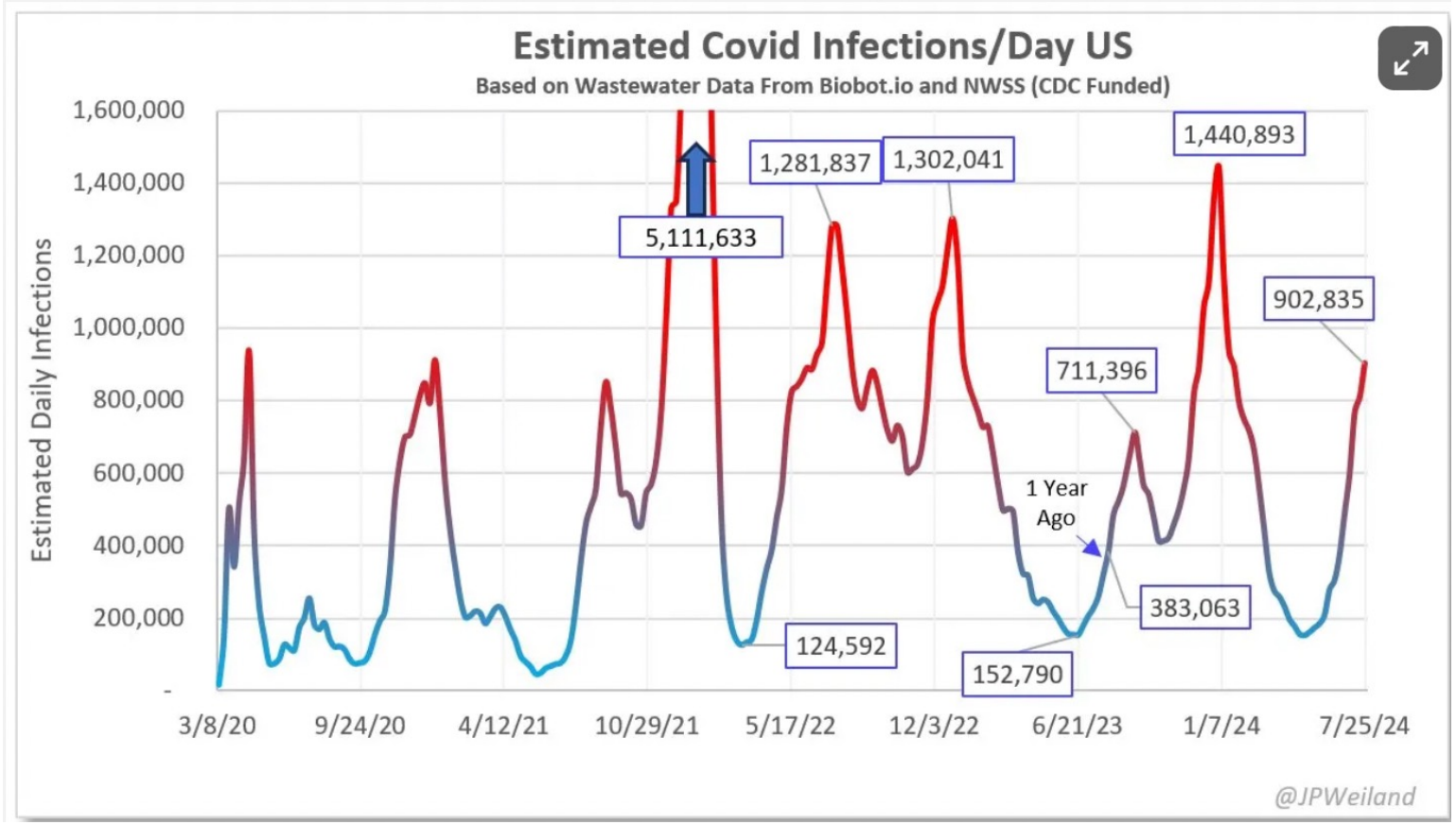




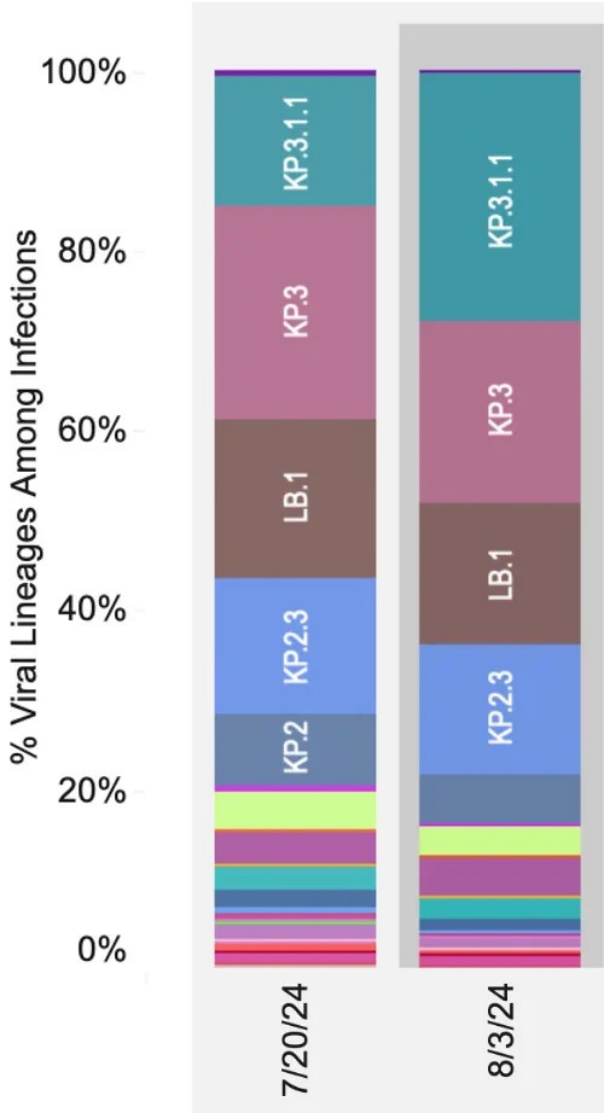
https://covid.cdc.gov/covid-data-tracker/#wastewater-surveillance

COVID-19: August 2024 Status

- Based on wastewater data, as many as 900K a day may be getting infected now.
- Hospitalizations and deaths due to COVID-19 are up but not nearly as high as earlier in pandemic.



COVID-19: August 2024 Status



- The current surge can be explained by seasonality (every summer we get an increase in cases) and the evolution of the virus to be more transmissible.
- While all the variants remain in the Omicron family, they have evolved from prior variants and gain better ability to spread.
- No evidence that current variants cause different or more severe disease.

COVID-19: August 2024 Status

- COVID-19 vaccines protect against:
  - Infection – May wane over weeks/months
  - Severe COVID-19 – Persists
  - Long COVID-19

- COVID-19 vaccines are among the safest vaccines we have.

- Updated vaccines for Fall 2024 are coming from Moderna and Pfizer. They will be mRNA vaccines that are designed to prompt a response to the KP.2 variant.

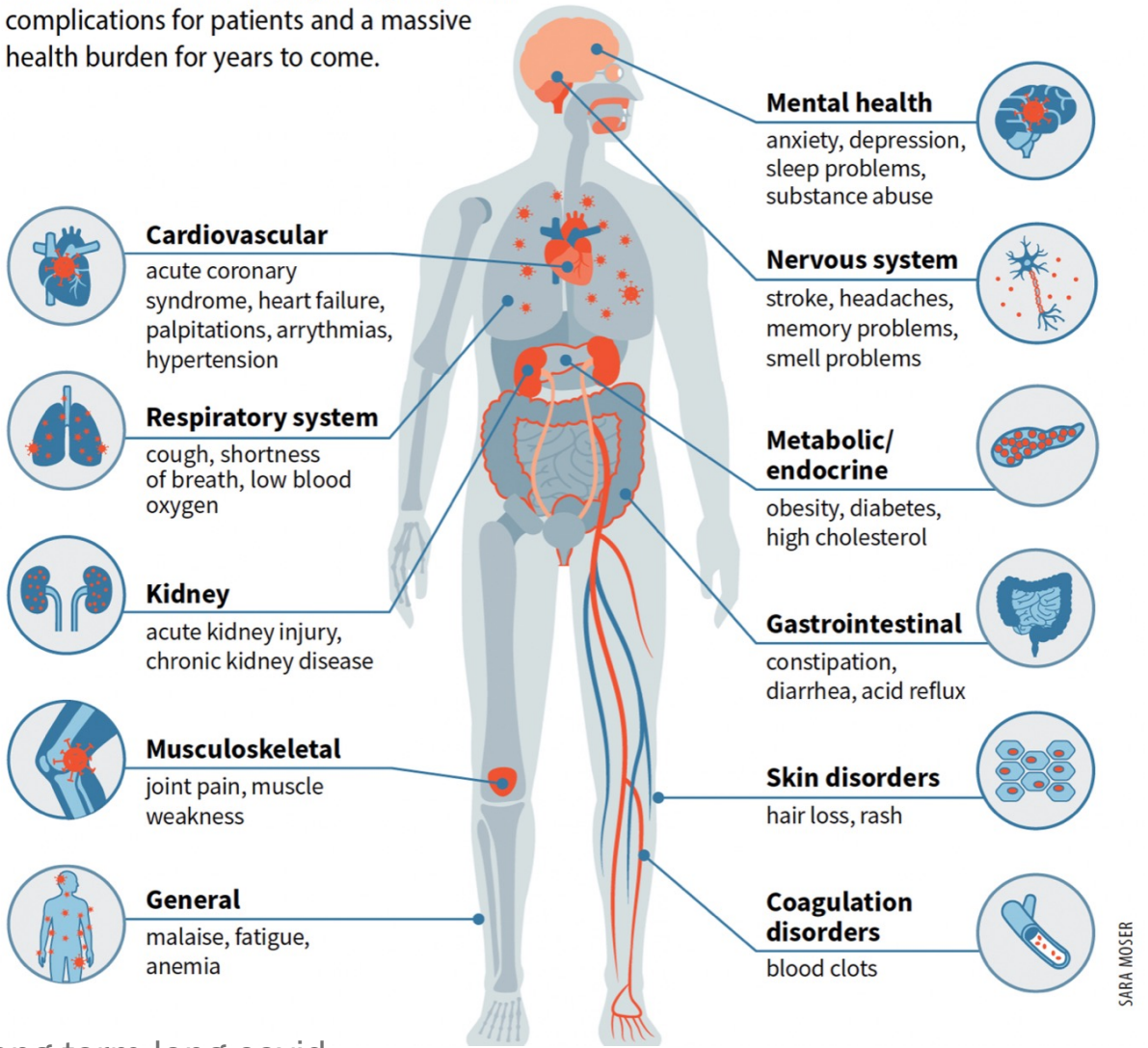
COVID-19: August 2024 Status

- In clinical trials earlier in the pandemic Paxlovid was found to protect people at high risk of severe disease from progression of COVID-19. Less data to support use in lower risk people.
- With better immunity, fewer may need an antiviral.
- Several studies find Paxlovid reduces risk of Long COVID.
- Best candidates for Paxlovid are:
  - Older people (75+)
  - Those who may expect their immune response to vaccination or prior infection to be weak
  - Pregnant people
  - Anyone who really wants it.

COVID-19: Lasting impact

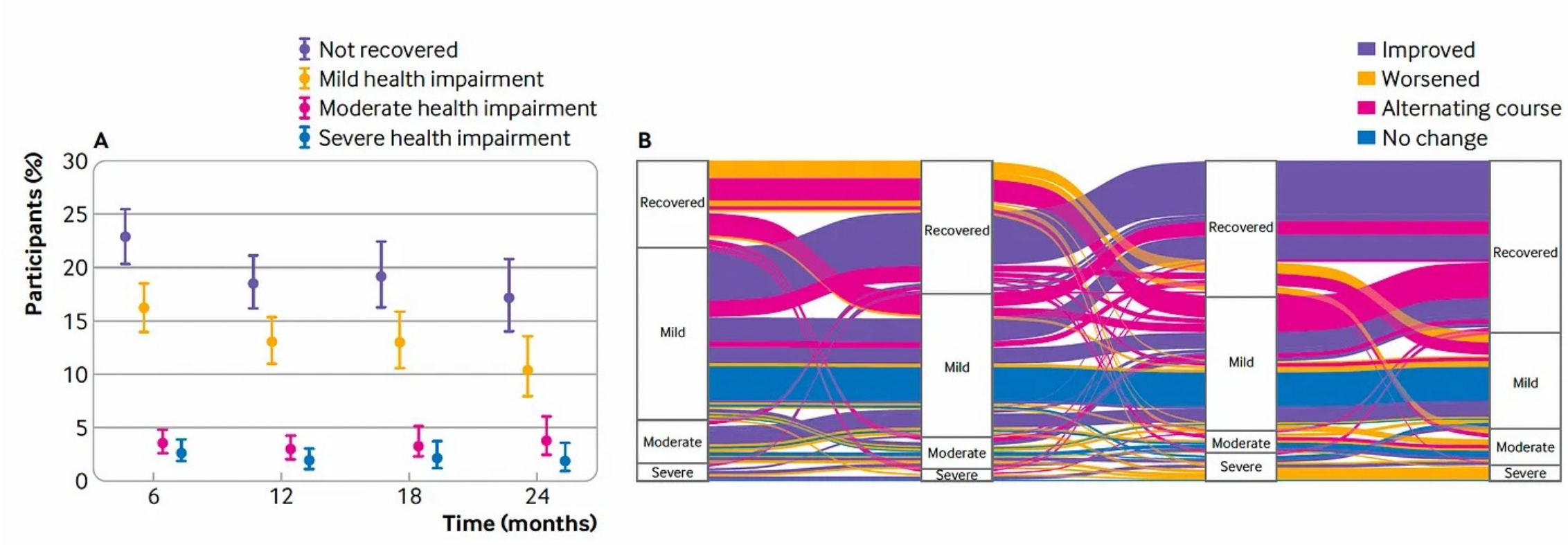
Even those survivors with mild initial cases can have wide-ranging health issues for ~~six months~~ two years or more.

WashU researchers have linked many diseases with COVID-19, signaling long-term complications for patients and a massive health burden for years to come.



https://erictopol.substack.com/p/long-term-long-covid

Long COVID-19 Trajectories



Longitudinal cohort study 1,106 people unvaccinated with COVID-19 in Zurich.
Decreasing rates of impairment but 18% not fully recovered at 2 years.

Ballouz T, et al. *BMJ* 2023;381:e074425

Why does this matter? COVID-19

- We are in a COVID-19 surge
- Largest summer surge
- New variants (KP.3) are more transmissible but not more deadly
- New vaccines are coming and will be better
- Paxlovid remains best treatment for those at high risk and perhaps to reduce Long COVID-19
- Masking works
- Long-COVID is major issue and is focus of belatedly intense study

MPOX

MPOX: August 2024 Status

The New York Times

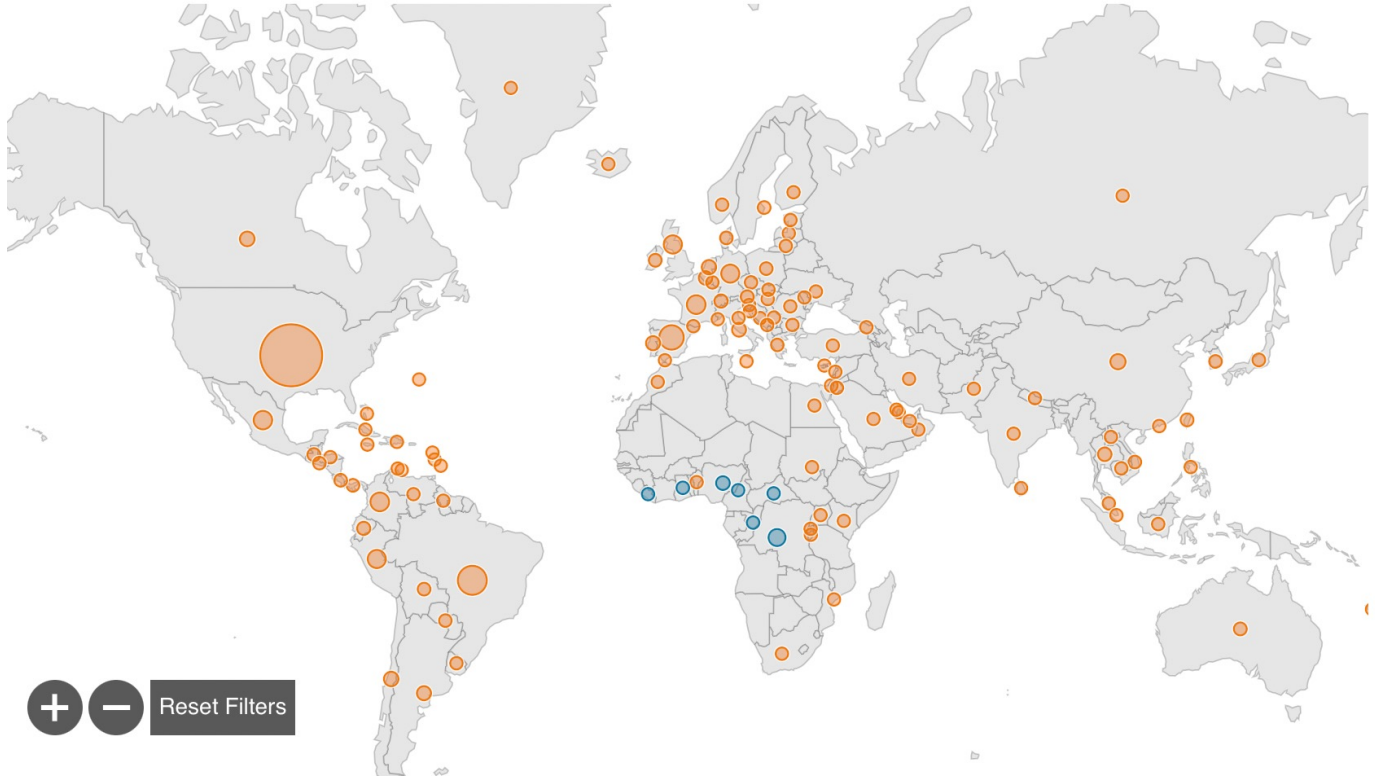
W.H.O. Declares Global Emergency Over New Mpox Outbreak

The epidemic is concentrated in the Democratic Republic of Congo, but the virus has now appeared in a dozen other African countries.

Share full article 136

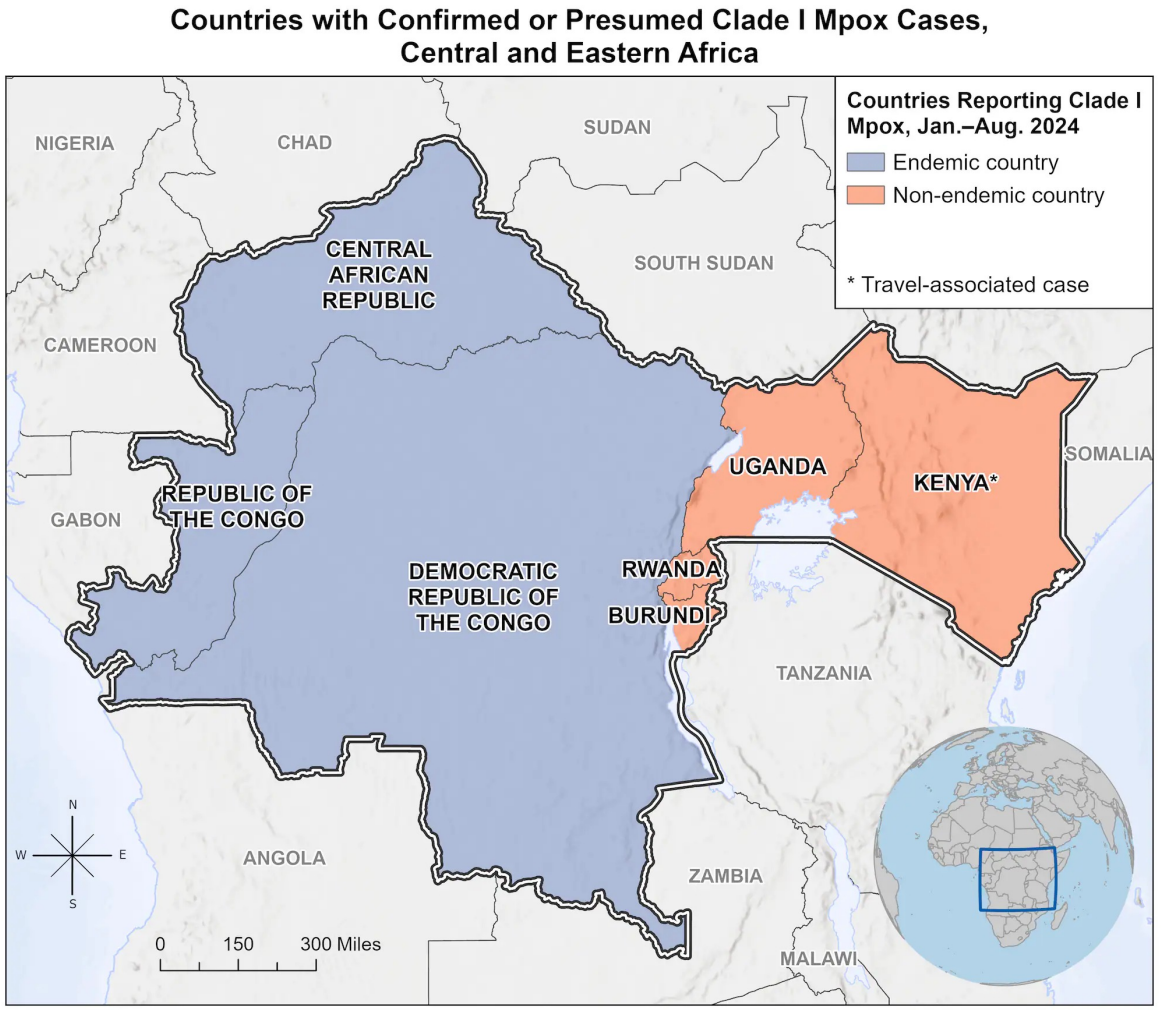
A laboratory nurse, with samples taken from a patient with a suspected case of mpox near Goma, Democratic Republic of Congo. Arlette Bashizi/Reuters

U.S. Cases	U.S. Deaths	Global Cases
Total Cases	Total Deaths	Total Cases
32,063	58	99,518

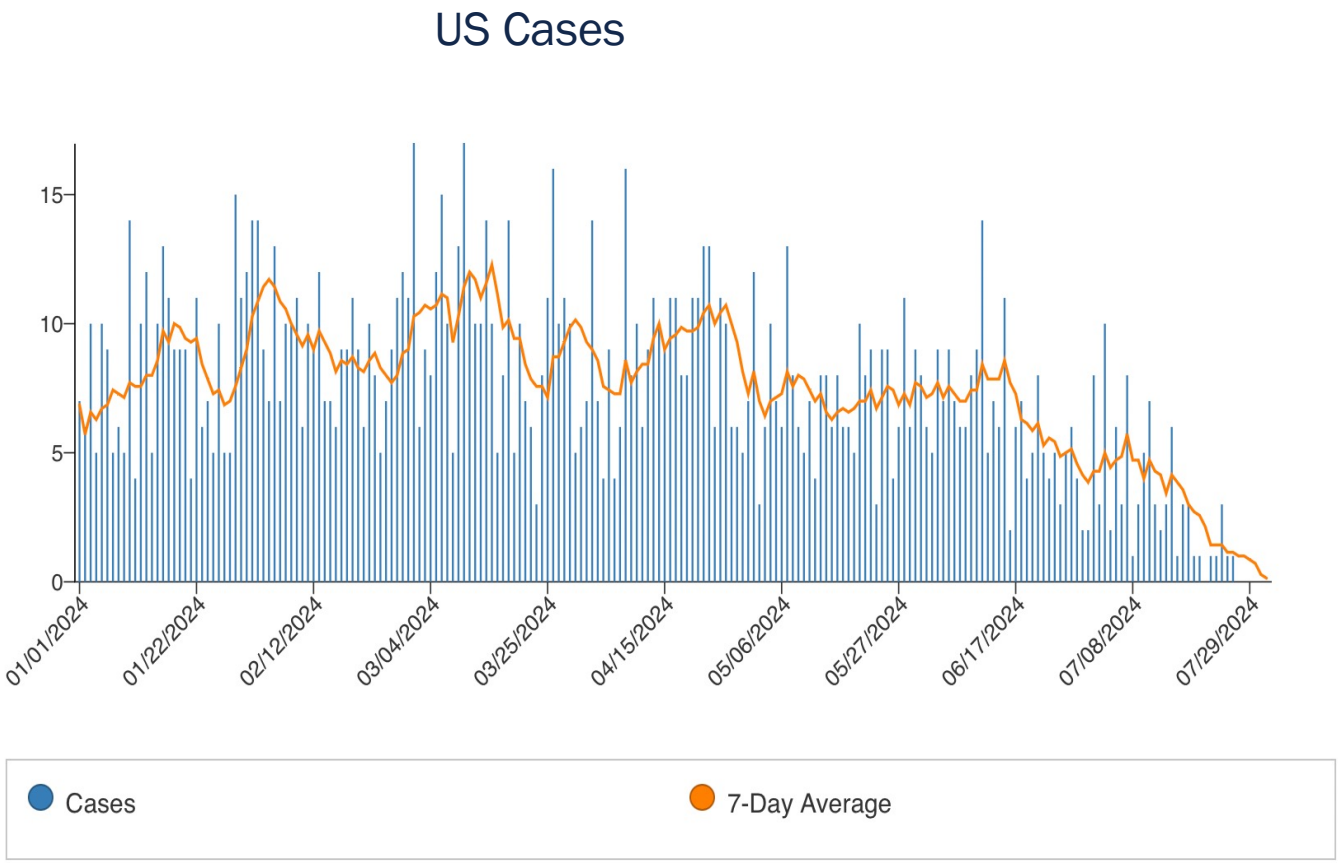


MPOX: August 2024 Status

- There are several outbreaks happening at the same time in DRC.
- In some provinces, patients have acquired infection through contact with infected dead or live wild animals, household transmission, or patient care (transmitted when appropriate PPE wasn't used or available)
  - a high proportion of cases have been reported in children younger than 15 years of age.
  - In other provinces, the cases are associated with sexual contact among men who have sex with men and female sex workers and their contacts.



MPOX: August 2024 Status



- Since January 2023, the Democratic Republic of the Congo (DRC) has reported more than **27,000** suspect mpox cases and more than **1,300** deaths.
- There are two types of mpox, **clade I** and **clade II**. Clade I usually causes a higher percentage of people with mpox to get severely sick or die compared to clade II.
- The current outbreak is more widespread than any previous DRC outbreak, and clade I mpox has spread to some neighboring countries, including Burundi, Central African Republic, Republic of the Congo, Rwanda, Uganda.
- A case of clade I has been reported in Sweden.

MPOX: August 2024 Status

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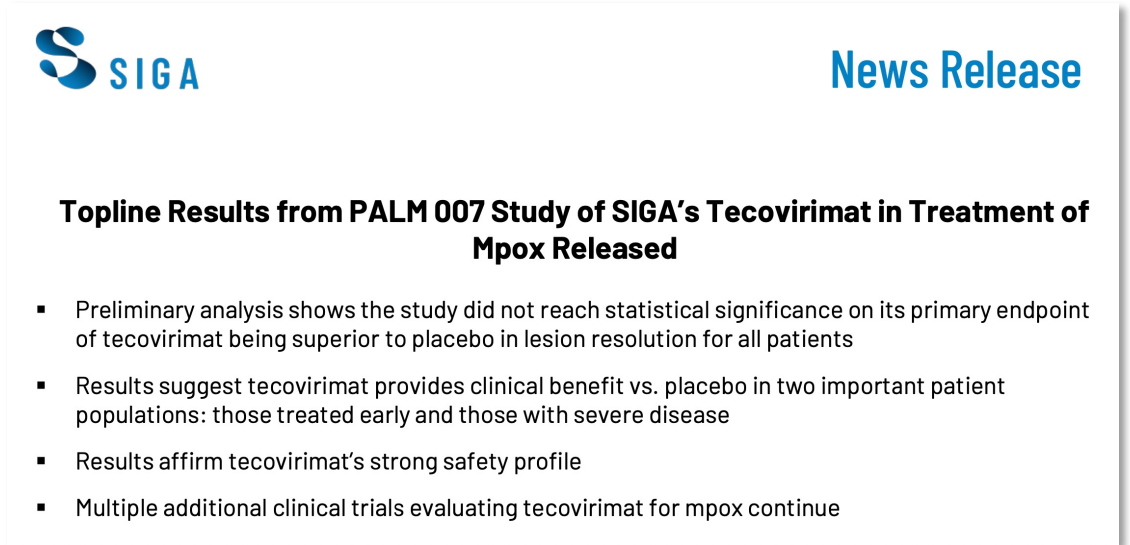
NEWS RELEASES

Thursday, August 15, 2024

The antiviral tecovirimat is safe but did not improve clade I mpox resolution in Democratic Republic of the Congo

NIH-cosponsored study examined tecovirimat in mpox-endemic country.



SIGA

News Release

Topline Results from PALM 007 Study of SIGA's Tecovirimat in Treatment of Mpox Released

- Preliminary analysis shows the study did not reach statistical significance on its primary endpoint of tecovirimat being superior to placebo in lesion resolution for all patients
- Results suggest tecovirimat provides clinical benefit vs. placebo in two important patient populations: those treated early and those with severe disease
- Results affirm tecovirimat's strong safety profile
- Multiple additional clinical trials evaluating tecovirimat for mpox continue

- Tecovirimat (TPOXX) has been used to treat mpox clade II but a recent NIH trial(PALM) conducted in DRC with patients infected with clade I did not show efficacy.
- Rates of mortality were lower than expected in both the TPOXX and placebo arms.
- Whether these results translate to other settings and populations or clade II is unknown.

MPOX: August 2024 Status

STOMP

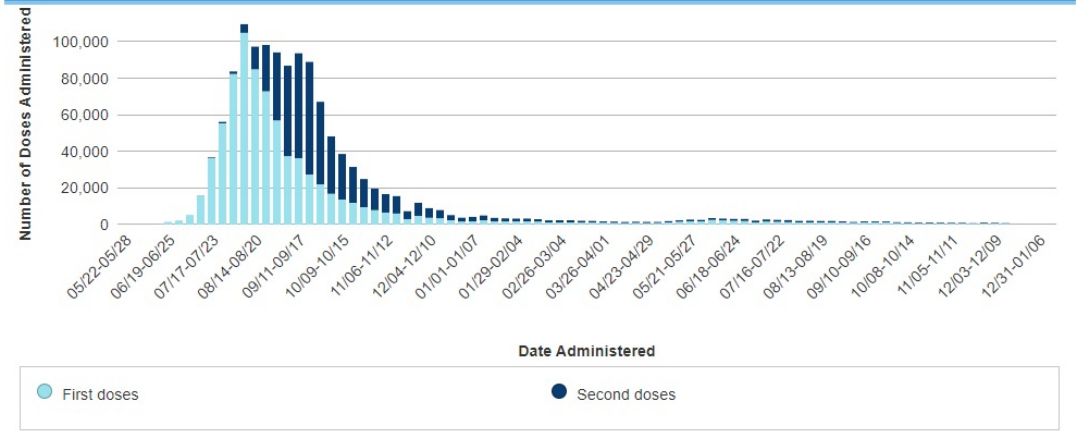
Study of Tecovirimat for Mpox

JYNNEOS VACCINE, US, CDC

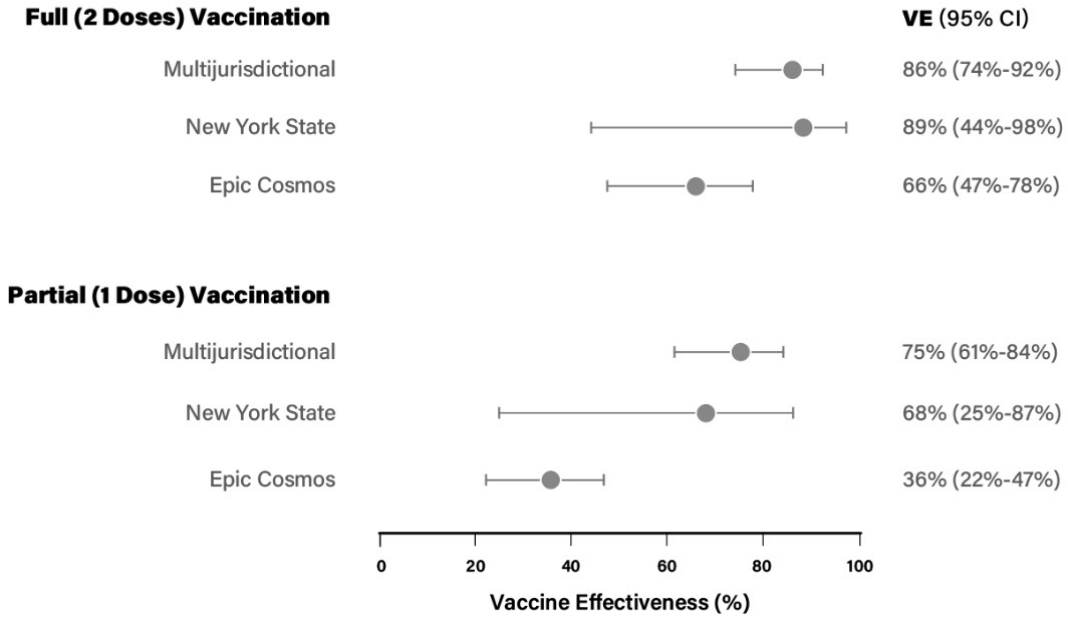
Total Vaccine Doses Administered

1,286,849
Doses Administered in the 57 U.S. Jurisdictions Reporting Data as of January 09 2024 .

Total JYNNEOS Vaccine Second Doses and First Doses Reported to CDC



Adjusted vaccine effectiveness (VE) of JYNNEOS vaccine against mpox by study and number of doses



JYNNEOS vaccine (the vaccine used in the current mpox outbreak) is effective at preventing mpox among people at risk of mpox. Although ~1.2 million vaccine doses have been administered, **only 23%** of the population at risk has been fully vaccinated nationally. Vaccine coverage varies widely between jurisdictions. Reasons for coverage variability could include lower vaccine accessibility and awareness, fewer vaccine providers, lower vaccine confidence and demand, and concern about stigma; https://www.cdc.gov/poxvirus/mpox/cases-data/mpx-jynneos-vaccine-coverage.html

Why does this matter? MPOX

- The rise in cases of clade I in DRC and other African nations is deeply concerning for the people in this region and for the potential of spread to other regions.
- Almost certainly we will see clade I in US.
- As clade II involved mostly MSM, need to be prepared to provide information to communities that can be impacted and healthcare providers.
- Vaccination should protect against clade II but need both shots.
- Whether TPOXX works is unclear, and all should be referred to the STOMP Trial.