AIDS 2024: Un resumen arbitrario

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Esta actividad es posible gracias al apoyo de

GSK × ViiV Healthcare

FUNDACIÓN HUÉSPED MEDIA PARTNER AIDS 2024

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PrEP

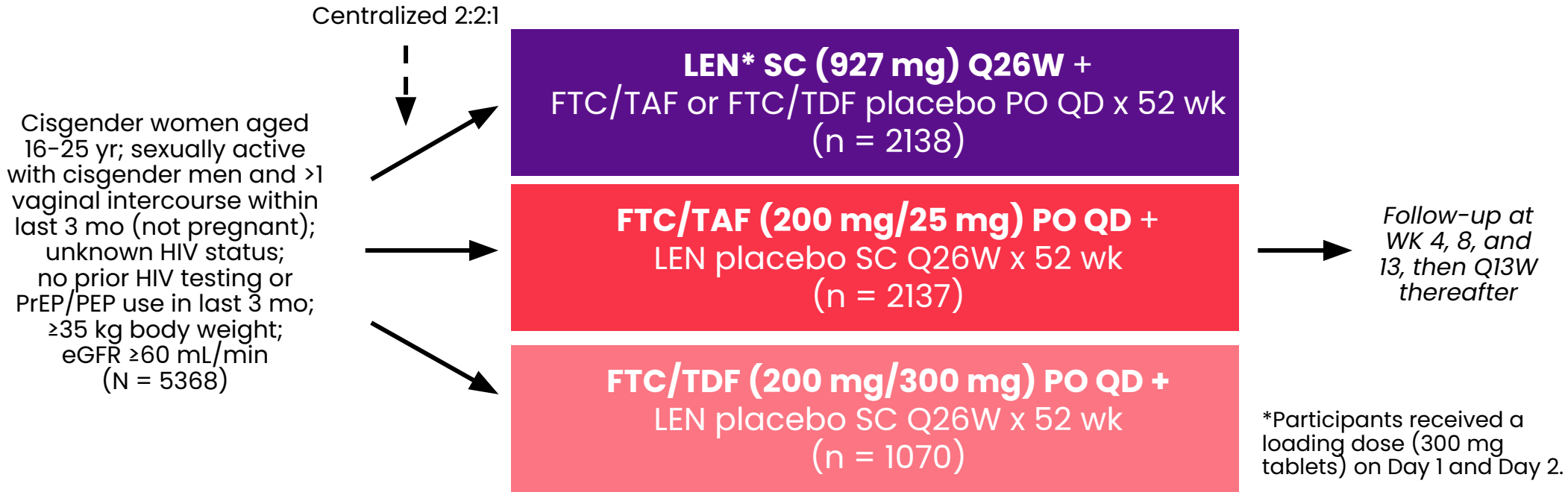
PURPOSE-1: **Background**

- Gaps remain with daily oral PrEP uptake, adherence, and persistence among cisgender women globally[1-3]
- Lenacapavir, an HIV-1 capsid inhibitor administered subcutaneously every 6 mo after loading dosage, has high potency and long half-life[4-5]
- FTC/TAF is noninferior to FTC/TDF for PrEP in cisgender men and transgender women who have sex with men[6]
- Current study compared efficacy and safety of twice yearly lenacapavir vs once-daily FTC/TAF as HIV prevention in adolescent girls and young women[8]
- Randomized blinded trial, South Africa & Uganda, > 5000 women 16-25 years, HIV negative, randomized 2:2:1 (LEN SC Q26W + oral F/TAF or F/TDF placebo (N = 2134); F/TAF qd + SC LEN placebo (N = 2136); F/TDF qd + SC LEN placebo (N = 1068)
- Prespecified interim analysis when 50% of participants completed ≥ 52 weeks:IDMC June 18th 2024: efficacy criteria met, discontinuation of study, switch from oral F/TXF to SC LEN

1. de Diu Tapsoba. AIDS Care. 2021;33:712. 2. Mugwanya. CROI 2024. Abstr 170. 3. Velloza. AIDS Behav. 2023;27:279. 4. Lenacapavir PI.
5. Segal-Maurer. NEJM. 2022;386:1793. 6. Mayer. Lancet. 2020;396:239. 8. Bekker. AIDS 2024. Abstr SS0407.

PURPOSE-1: **Study Design**

- Multicenter, double-blind, active-controlled, randomized phase III trial in South Africa and Uganda*

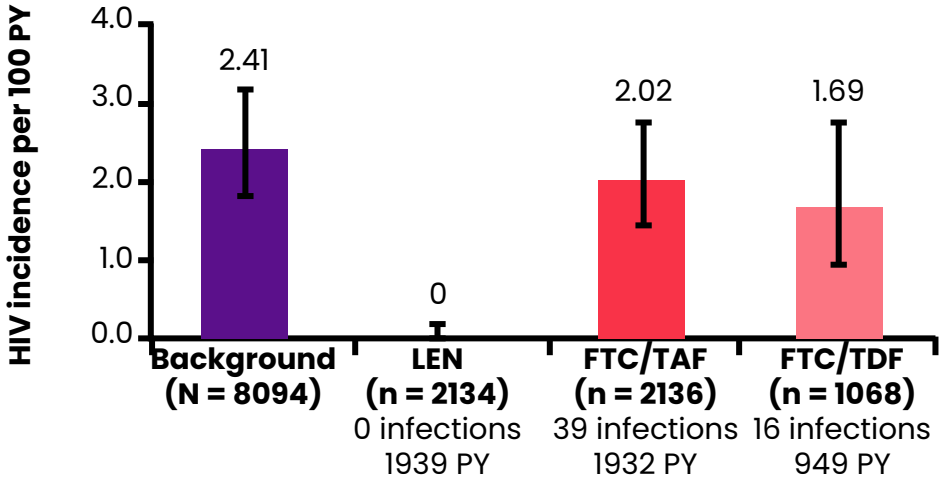


- Primary endpoint: HIV incidence at screening and follow-up, compared with incidence in screened but unenrolled persons as no-PrEP observational group
- Key secondary endpoints: HIV incidence vs incidence in FTC/TDF group, adherence, safety

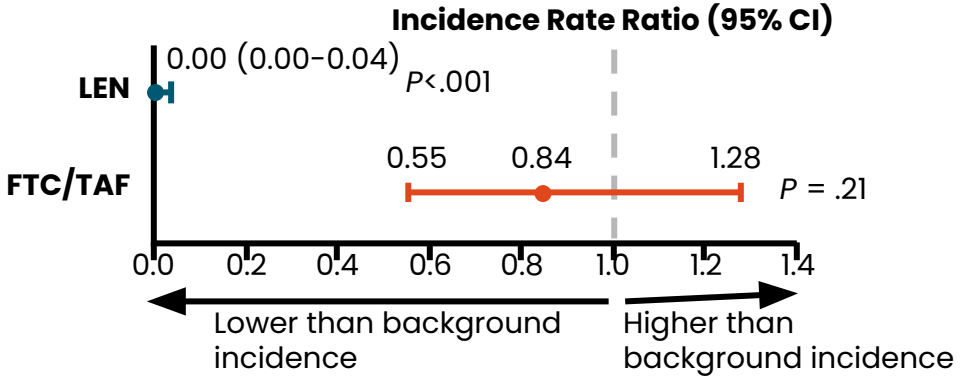
NCT04994509. Bekker. AIDS 2024. Abstr SS0407. Bekker. NEJM. 2024;[Epub].

PURPOSE-1: **HIV Incidence**

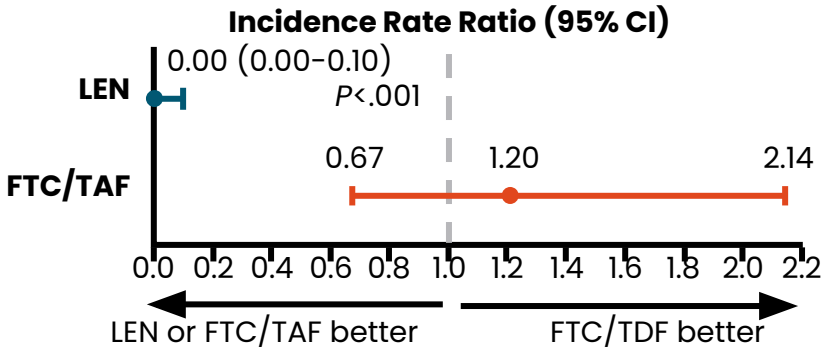
HIV Incidence: Background vs Follow-up



Primary Endpoint: HIV Infection IRR vs Background



Secondary Endpoint: HIV Infection IRR vs FTC/TDF



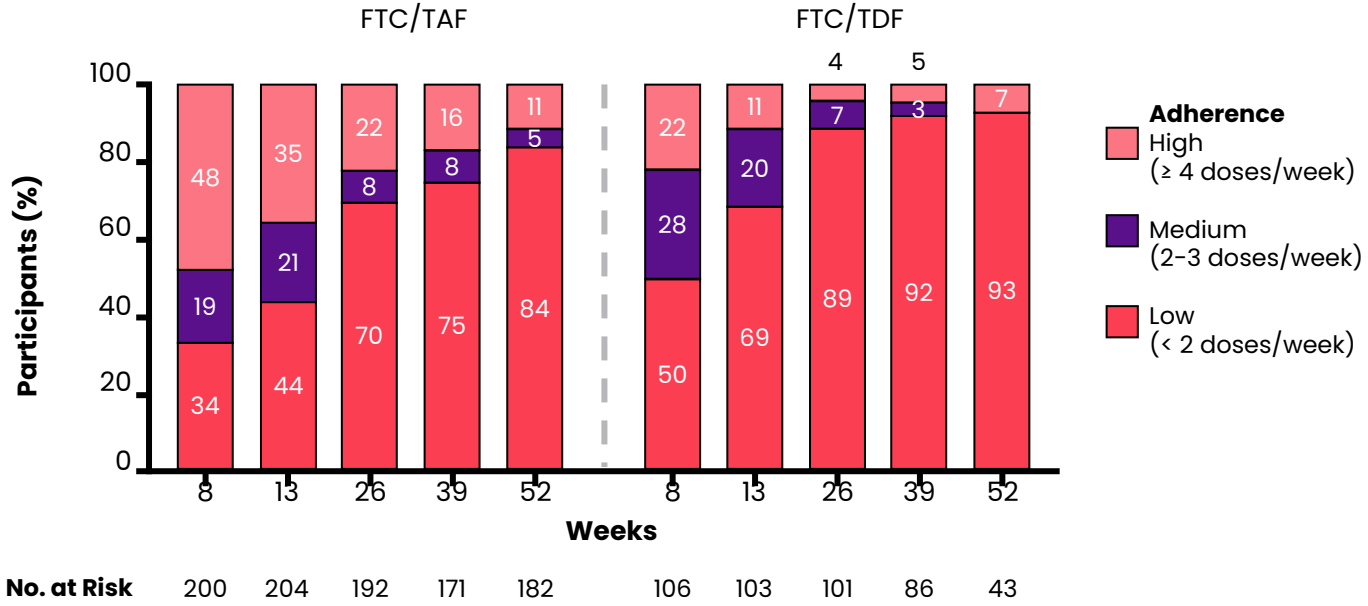
- No HIV infections in LEN group
- IRR with LEN significantly lower than background incidence or FTC/TDF incidence
- IRR with FTC/TAF not significantly different from background incidence or FTC/TDF incidence
  - Injection site reactions common in lenacapavir arm (led to only 4 discontinuations)

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

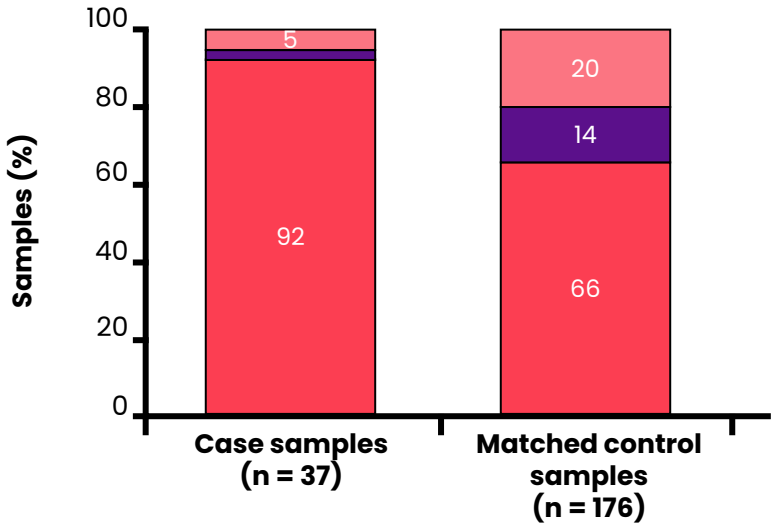
PURPOSE-1: **Adherence**

- On-time injections were similar across all groups: 91.5% at Wk 26 and 92.8% at Wk 52
- Adherence to oral therapy was low for most FTC/TAF and FTC/TDF participants and decreased over time

Adherence to FTC/TAF and FTC/TDF



FTC/TAF Adherence-Efficacy Association



- Lower odds of HIV infection with medium or high FTC/TAF adherence vs low adherence (OR: 0.11; 95% CI: 0.01 to 0.49)

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

PURPOSE-1: **Pregnancies**

Event	LEN (n = 2138)	FTC/TAF (n = 2137)	FTC/TDF (n = 1070)
Patients with confirmed pregnancy, n	184	208	95
Confirmed pregnancies, n	193	219	98
Pregnancy status, n (%)			
▪ Completed	105 (54.4)	119 (54.4)	53 (54.1)
▪ Ongoing	88 (45.6)	100 (45.7)	45 (45.9)
▪ Births	55 (28.5)	45 (20.5)	21 (21.4)
▪ Induced abortion	30 (15.5)	40 (18.3)	20 (20.4)
▪ Spontaneous miscarriage	20 (10.4)	34 (15.5)	12 (12.2)

- Outcomes were similar to those expected for the study population
- Rates of expected spontaneous miscarriage: 10%-20% clinically recognized, ~30% biochemically detected

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

PURPOSE-1: **Investigators' Conclusions**

- In cisgender women without prior HIV infection, PrEP with twice-yearly SC LEN resulted in no infections
- HIV incidence with LEN was significantly lower than background and FTC/TDF incidence
- Adherence to PrEP with oral FTC/TAF and FTC/TDF was poor
- Medium or high FTC/TAF adherence associated with lower odds of HIV infection
- SC LEN and oral FTC/TAF were well tolerated and safe

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

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Estrategias De TARV

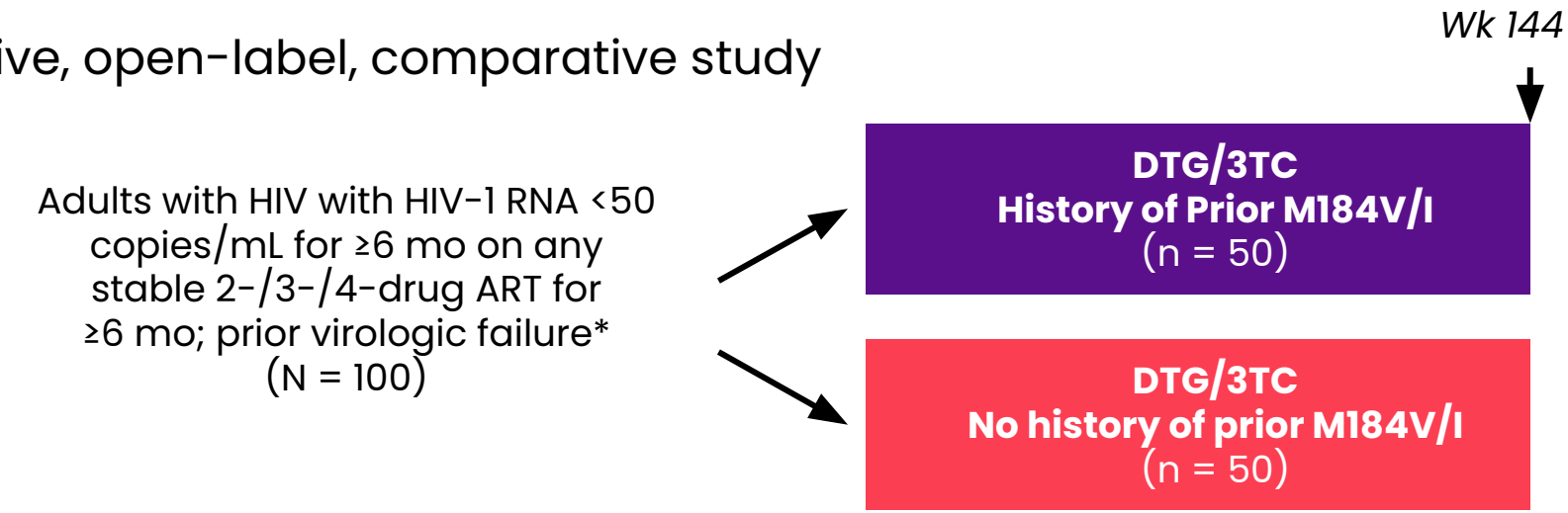
SOLAR-3D: **Background**

- DTG/3TC not approved for switch in people with HIV with history of DTG and/or 3TC resistance, or prior VF1-3
- Insufficient data on whether DTG/3TC can maintain HIV-1 RNA <50 copies/mL in virologically suppressed individuals switching ART with prior/current M184V/I and/or VF
- Recent data suggest that switching to DTG/3TC can maintain virologic suppression in 96%-100% of people with HIV at Wk 48-96 despite prior/current archived 3TC RAMs and VF4-8
- Current study evaluated the efficacy and safety of switching to DTG/3TC in heavily treatment–experienced people with HIV who are virologically suppressed9

1. Van Wyk. Clin Infect Dis. 2020;71:1920. 2. DHHS HIV Guidelines. 2021. 3. EACS HIV Guidelines. 2020. 4. Rial-Crestelo. J Antimicrob Chemother. 2021;76:738. 5. Madhusudan. Open Forum Infect Dis. 2023;10:ofad526. 6. Blick. IAS 2023. Abstr OAB0202. 7. De Miguel.
EACS 2023. Abstr ep.A.097. 8. De Miguel. CROI 2024. Abstr 693. 9. Blick. AIDS 2024. Abstr SS0403LB.

SOLAR-3D: **Study Design**

- 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)

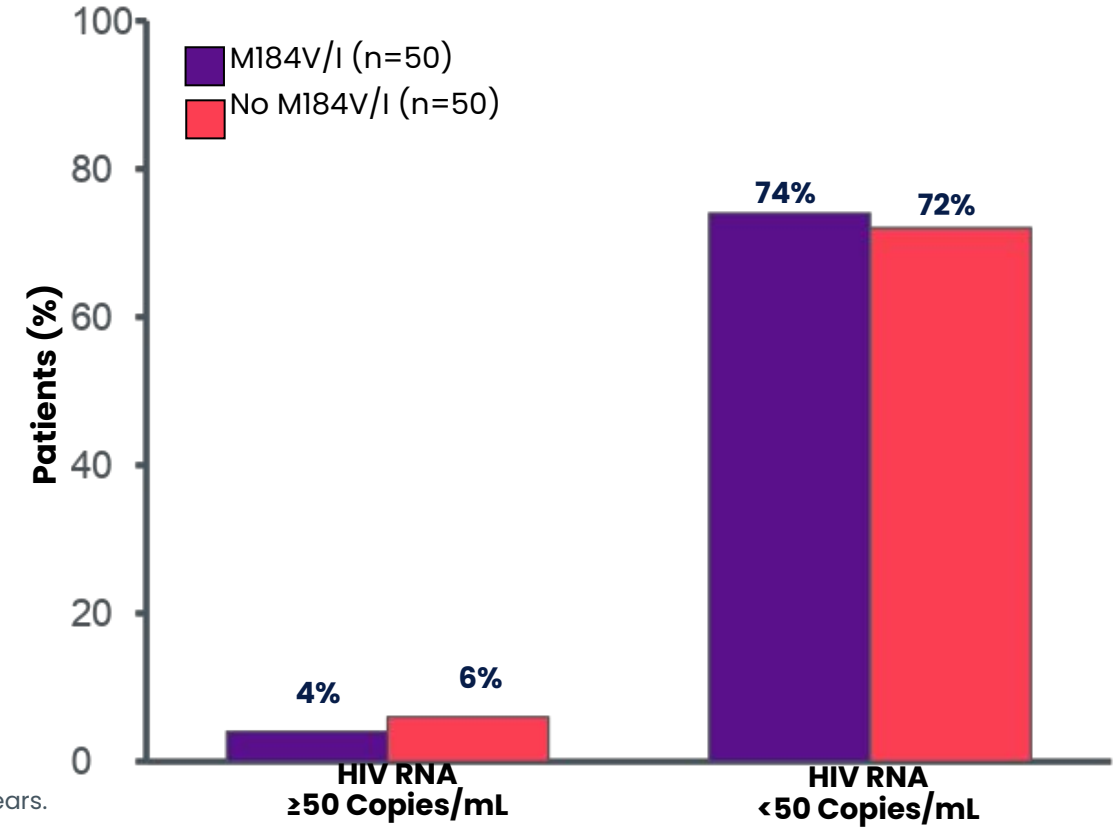
- Secondary endpoints: HIV-1 RNA <50 copies/mL at Wk 48 and 96 (FDA Snapshot, ITT-E, per protocol), discontinuations resulting from CVF (HIV-1 RNA ≥50 copies/mL followed by HIV-1 RNA ≥200 copies/mL)

Blick. AIDS 2024. Abstr SS0403LB.

SOLAR-3D **Study:** Switch to Dolutegravir/3TC in Patients With Prior Virologic Failure and Historic M184V/I Mutation

- **Prospective, open-label study**
  - Treatment-experienced patients on stable 3- or 4-drug ART (HIV RNA <50 copies/mL for ≥6 months)
  - Prior historic M184V/I mutation and prior virologic failure (HIV RNA >200 copies/mL)
- **Results at week 144 after switching to dolutegravir/3TC**
  - Similar rate of HIV RNA <50 copies/mL regardless of prior M184V/I
  - Confirmed virologic failure: M184V/I (n=0) and no M184V/I (n=1 due to adherence) arms
  - No difference in incidence of viral blips

Virologic Outcomes at Week 144 (ITT-E)



Baseline characteristics:
Time since HIV diagnosis: 25 years.
ART duration: 22 years.
Previous number of ART regimens: 7.

Blick G, et al. IAS 2024. Abstract SS0403LB.

SOLAR-3D: **Investigator's Conclusions**

- Switching treatment-experienced, virologically suppressed people with HIV to DTG/3TC was effective and durable through 144 wk despite prior VF and prior or current M184V/I

- No participants discontinued treatment for CVF

Blick. AIDS 2024. Abstr SS0403LB.

D2EFT: **Background**

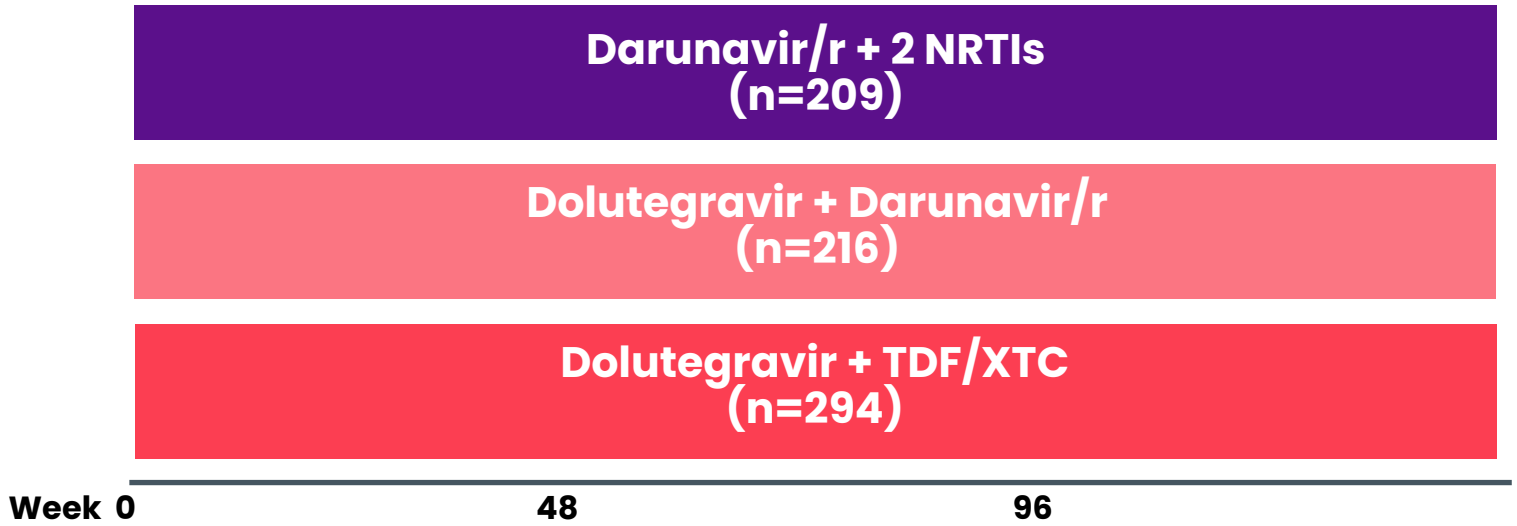
- Randomized trial data on efficacy and safety of second-line ART after treatment failure with first-line NNRTI-based ART is limited[1]
  - In 2017, standard of care for second-line regimen was **RTV-boosted PI** + 2 NRTIs[2]
  - Current guideline-recommended second-line regimens also include **DTG** + 2 NRTIs[1]
- In people with HIV whose first-line NNRTI-based ART failed, phase IIIb/IV D^{2}EFT trial compared 2 **DTG**-based second-line ART regimens vs standard of care DRV/RTV + 2 NRTIs[3,4]
  - Initial Wk 48 results showed that **DTG + DRV/RTV** *and* **DTG (3TC or FTC)/TDF** were *noninferior* to standard of care; further, **DTG + DRV/RTV** was *superior* to standard of care
  - Current analysis reports final outcomes at 96 wk[5]

1. clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/virologic-failure-and-antiretroviral?view=full. 2. NCT03017872
3. Matthews. Lancet HIV. 2024;11:e436. 4. Matthews. CROI 2024. Abstr 198. 5. Kumarasamy. AIDS 2024. Abstr OAB3804.

D2EFT Study: Dolutegravir- Versus Darunavir/r-Based ART for Patients Failing First-Line NNRTI-Based ART

Phase 4

Open-label
Failed first-line NNRTI + 2 NRTIs
No prior PI/INSTI
HBsAg negative
No significant comorbidities or active coinfection
Not pregnant



D²EFT: Dolutegravir and darunavir evaluation in adults failing therapy.
Primary endpoint: HIV RNA <50 copies/mL at week 48 and 96.
Baseline characteristics:
Age (mean): 39 years.
Male: 46%.
BMI: 23 kg/m^2.
CD4: 206 cells/µL.

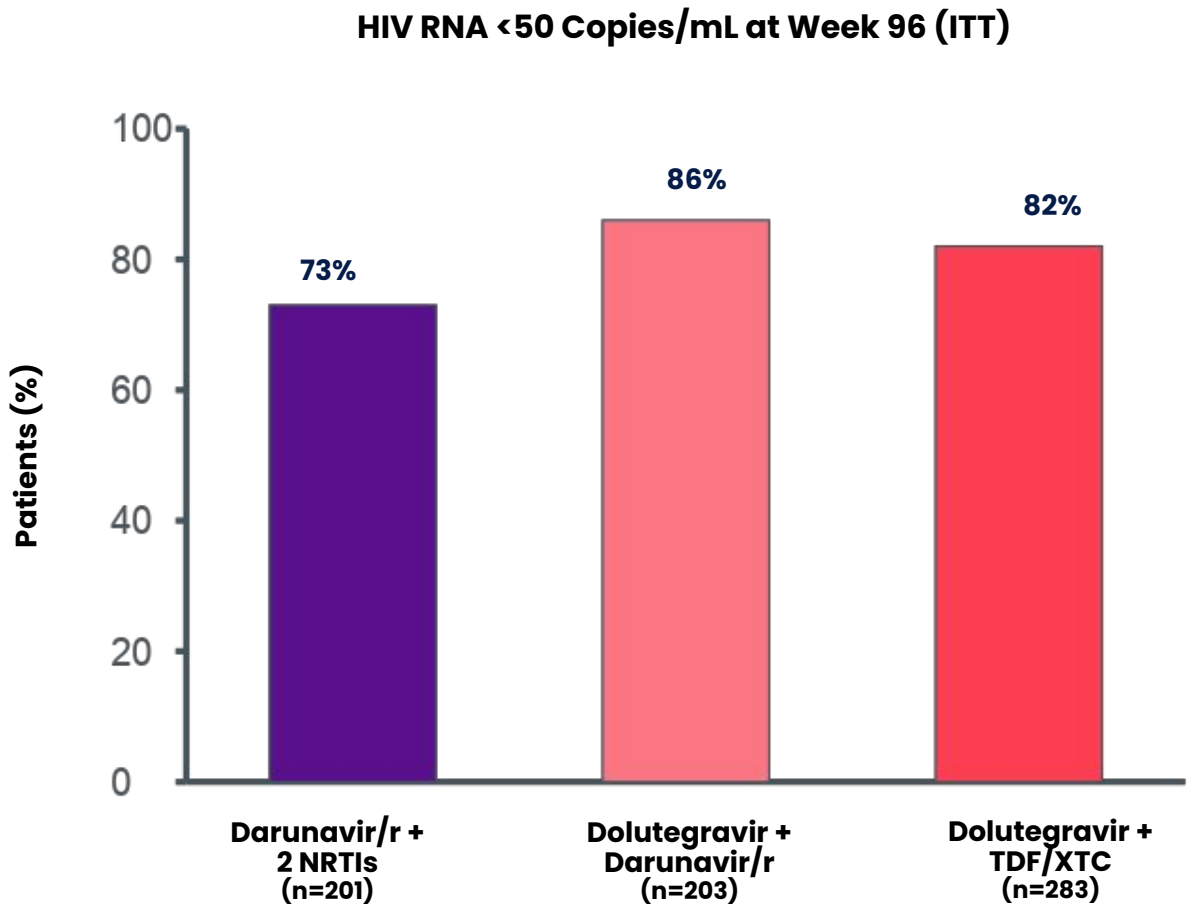
- **Primary endpoint:** HIV-1 RNA <50 c/mL in mITT at Wk 48
- **Key secondary endpoints:** HIV-RNA <200 c/mL, change in CD4+ cell count, and safety at Wk 48 and 96

Current Analysis

Kumarasamy N, et al. AIDS 2024. Abstract OAB3804.

D2EFT Study: **Outcomes at Week 96**

- Both dolutegravir arms were non-inferior to darunavir/r + 2 NRTIs with regard to HIV RNA <50 copies/mL
  - Dolutegravir + darunavir/r met superiority criteria
- Significant mean weight gain in both dolutegravir arms compared with darunavir/r + 2 NRTIs
  - Dolutegravir + darunavir/r (+4.1 kg; *P*<0.01)
  - Dolutegravir + TDF/XTC (+5.8 kg; *P*<0.01)



Kumarasamy N, et al. AIDS 2024. Abstract OAB3804.

D2EFT: **Investigator's Conclusions**

- As second-line treatment after NNRTI-based ART failure, both **DTG + DRV/RTV** *and* **DTG + TDF + (3TC or FTC)** were superior to **DRV/RTV + 2 NRTIs** in achieving virologic suppression and immunological recovery through 96 wk
  - In DTG + TDF + (3TC or FTC) second-line regimen, recycling of TDF was efficacious, even without genotyping
- All treatment combinations were well tolerated; few switches due to toxicity
  - Both DTG-containing regimens associated with greater weight gains than DRV/RTV + 2 NRTIs

Kumarasamy. AIDS 2024. Abstr OAB3804.

PASO-DOBLE: **Background**

- In current treatment paradigm, ART is a lifelong requirement to control HIV
  - Efforts to optimize ART regimens for simplicity and tolerability both in first-line regimens and in later regimens are key for maintaining quality of life
- DTG/3TC and BIC/FTC/TAF are preferred first-line regimens and are also recommended by guidelines as switch regimens in persons with virologic suppression in certain cases[1-3]
  - Role of DTG, BIC, TAF in potential weight gain unclear
- Current study compares the safety and tolerability (including weight gain) of DTG/3TC and BIC/FTC/TAF as switch regimens for persons with virologic suppression[4]

1. DHHS Guidelines ART 2024. 2. EACS AIDS Guideline v. 11.1. 2022. 3. Ghandi. JAMA. 2023;329:63. 4. Martinez. AIDS 2024. Abstr OAB3606LB.

PASO-DOBLE: **Study Design**

- 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)

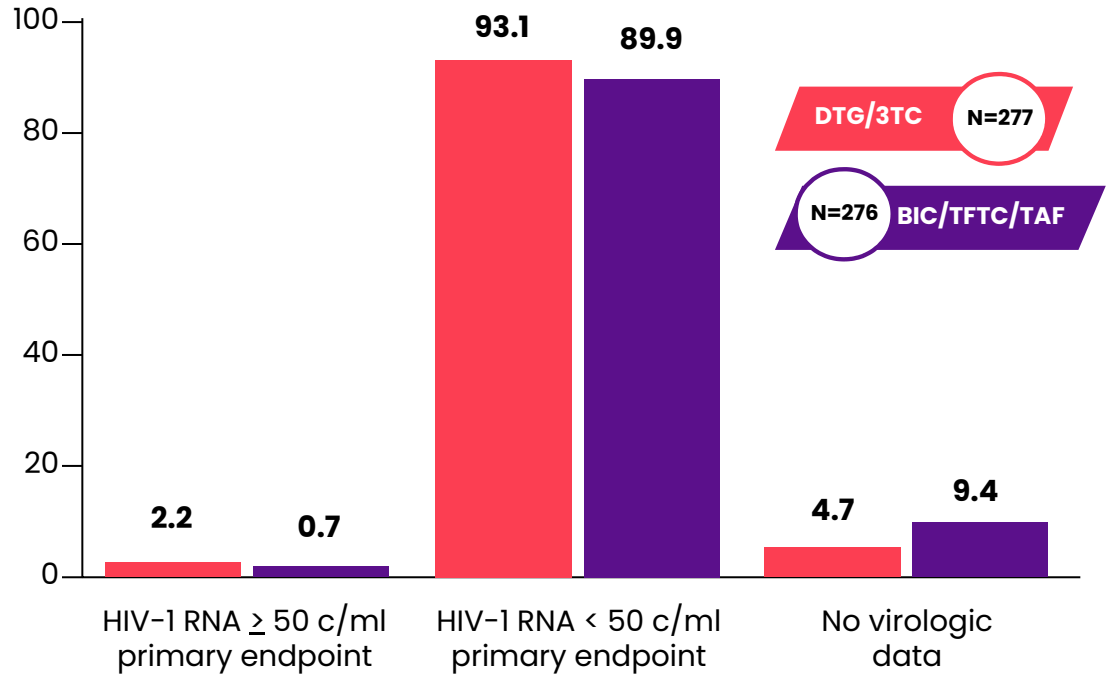
BIC/FTC/TAF
(n = 276)

- 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.

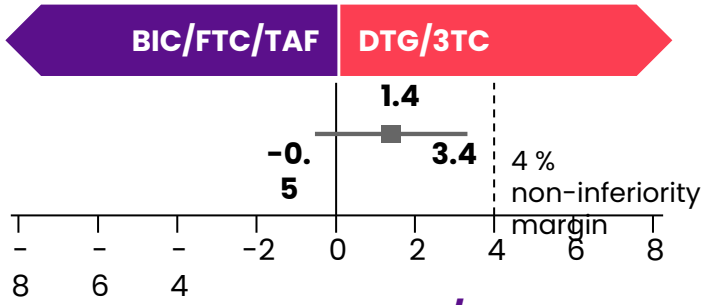
Switch to DTG/3TC vs BIC/F/TAF in virologically suppressed PWH: PASO-DOBLE trial *(2)*

Snapshot outcomes at week 48 (ITT-E population)

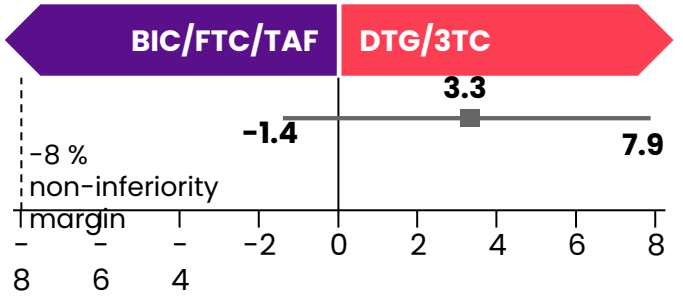


No emergence of resistance

HIV-1 RNA ≥ 50 c/ml



HIV-1 RNA < 50 c/ml



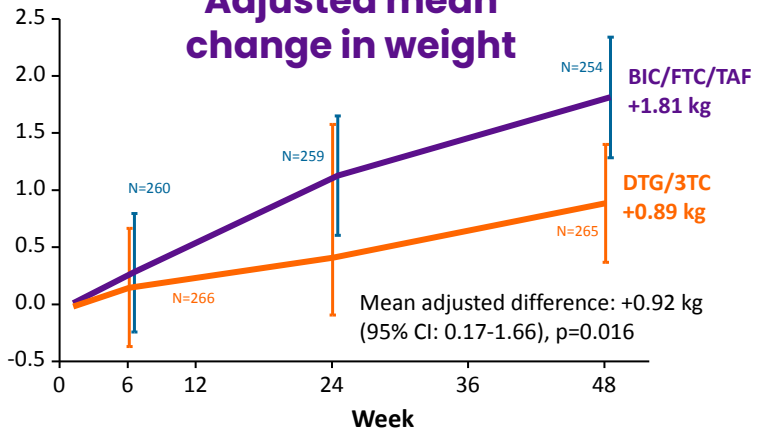
Difference in proportion of participants, % (95% CI)

Non-inferiority demonstrated

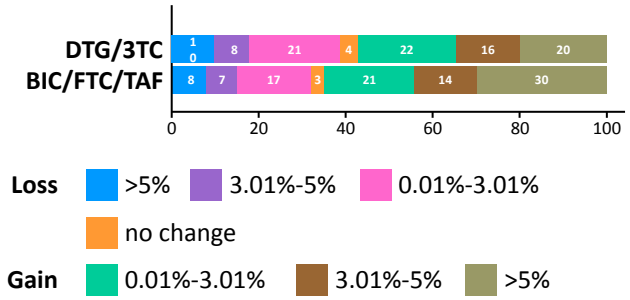
Ryan P, et al. AIDS2024 ; # OAB3606LB

Switch to DTG/3TC vs BIC/F/TAF in virologically suppressed PWH: PASO-DOBLE trial *(3)*

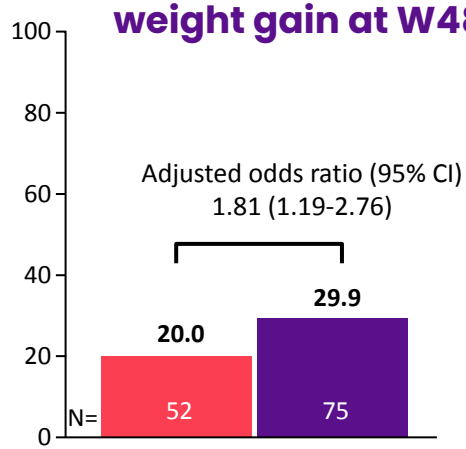
Adjusted mean change in weight



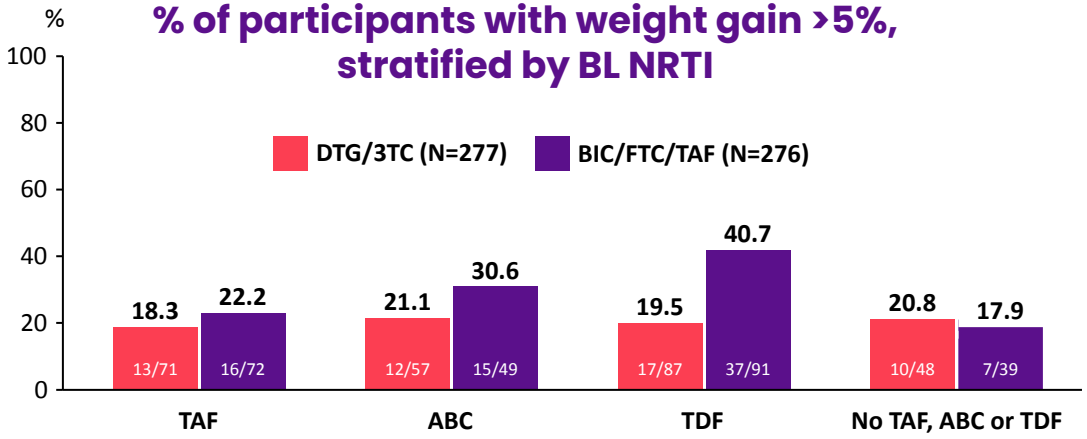
% weight change strata at W48



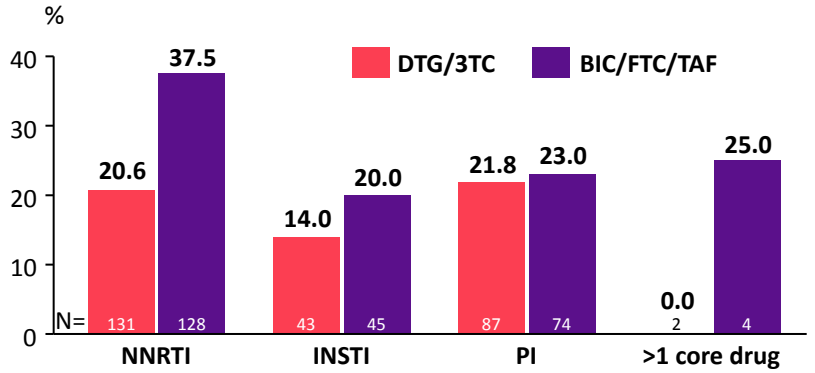
% of participants with >5% weight gain at W48



% of participants with weight gain >5%, stratified by BL NRTI



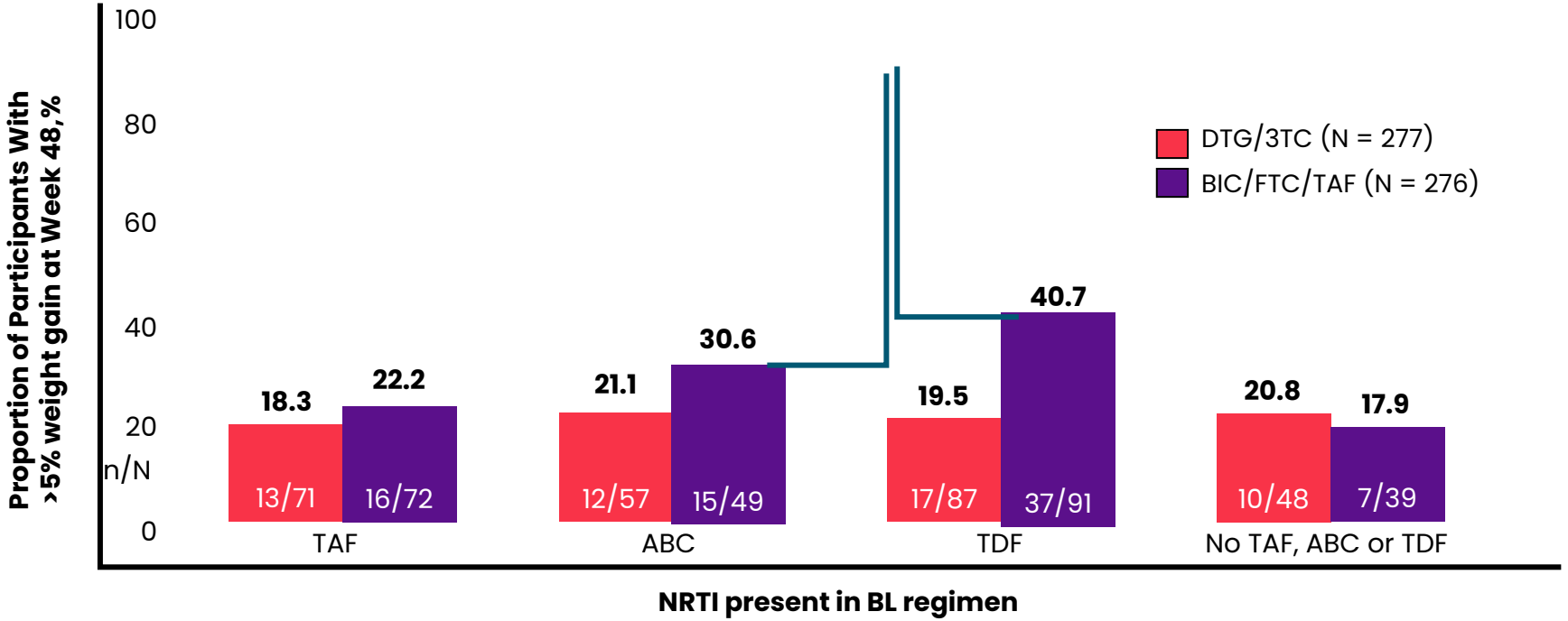
% of participants with weight gain >5%, stratified by BL core ARV



Ryan P, et al. AIDS2024 ; # OAB3606LB

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.

PASO-DOBLE (GeSIDA 11720): **Investigators' Conclusions**

- In persons with HIV who are virologically suppressed on ART, switch ART to DTG/3TC was noninferior to switch to BIC/FTC TAF in terms of virologic efficacy
  - DTG/3TC and BIC/FTC/TAF had similar high barriers to resistance
  - Both regimens were well tolerated, with few discontinuations due to adverse effects
- Switch to BIC/FTC/TAF led to significantly more weight gain than switch to DTG/3TC
  - Extent of weight gain may depend on prior ART regimen and core drug

Martinez. AIDS 2024. Abstr OAB3606.

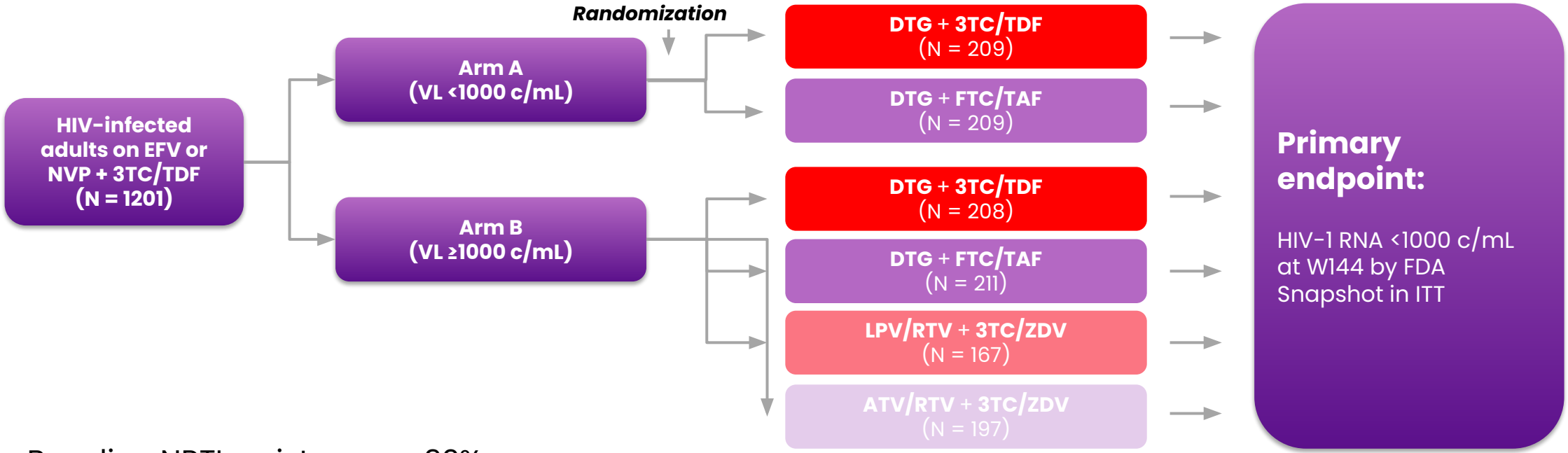
VISEND: **Background**

- When a switch to second-line ART is warranted, WHO recommends optimization of NRTIs from TFV analogues or ABC to thymidine analogues[1]
  - In low- or middle-income countries, HIV drug resistance testing upon first-line failure not readily available
- After failure of NNRTI-based ART, lack of data on long-term outcomes of switch to DTG-based regimens with maintained NRTI backbone
  - In VISEND Wk 48 analysis, favorable virologic outcomes observed with switch to DTG + either 3TC/TDF or FTC/TAF[2]
- Current study evaluated Wk 144 results of switch to DTG plus recycled NRTIs after virologic failure of NNRTI-based regimens[3]

1. WHO. Update of recommendations on first- and second-line antiretroviral regimens. 2019.
2. Mulenga. CROI 2022. Abstr 135. 3. Sivile. AIDS 2024. Abstr OAB3806LB.

VISEND: **DTG + recycled NRTI vs bPI + 3TC/ZDV for Second-line Therapy *(1)***

- Randomized, open-label, noninferiority phase III trial in Zambia

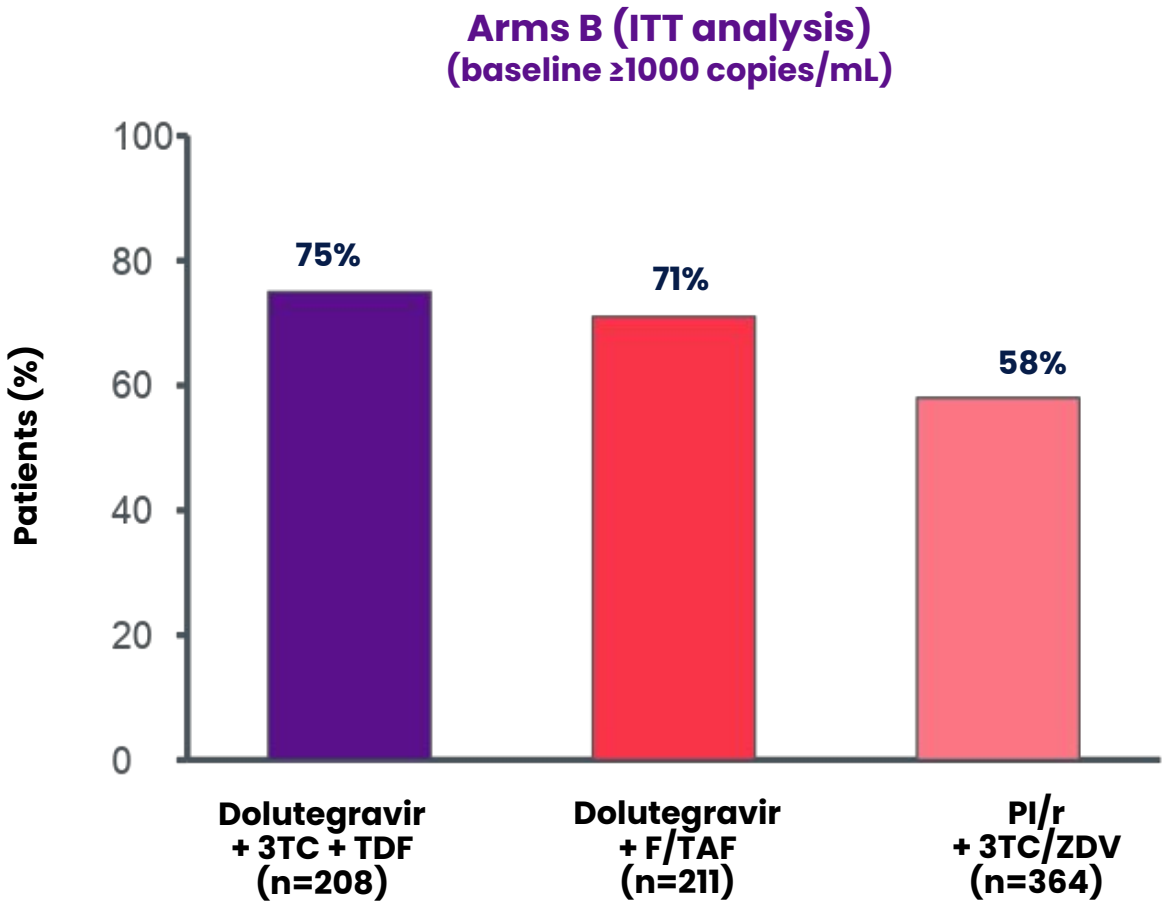


- Baseline NRTI resistance = 92%
  - In those randomized to TXF/XTC/DTG: 57% had no predicted TFV activity, 75% no predicted XTC activity
  - In those randomized to AZT/3TC/bPI: 46% had ≥ 1 AZT mutations

Sivile S, et al. AIDS2024 ; # OAB3806LB

VISEND Trial: **HIV RNA <1000 Copies/mL (ITT) at Week 144 After Switch**

- Switching to dolutegravir + 3TC + TDF was non-inferior to dolutegravir F/TAF
  - No emergence of dolutegravir resistance
- Switching to dolutegravir-based regimens was superior to PI/R-based regimens



VISEND: Virological Impact of Switching From Efavirenz and Nevirapine Based First-Line ART Regimens to Dolutegravir.

Sivile S, et al. AIDS 2024. Abstract OAB3806LB.

VISEND: **Investigator's Conclusions**

- After virologic failure of NNRTI + TDF/XTC, switch to DTG plus either 3TC/TDF or FTC/TAF was associated with favorable outcomes vs switch to standard-of-care PI-based ART at 144 wk
  - High rates of virologic suppression despite high baseline NRTI resistance
  - No resistance to DTG observed

Sivile. AIDS 2024. Abstr OAB3806LB.

Dolutegravir + Doravirine (DoDo)

- Descriptive analysis, patients in Germany and Austria (8 sites)
- Unique profile of patients treated with DoDo (N = 106)
  - Extensively pretreated (median 21 years, median 6 previous regimens)
  - Median age 58 years
  - Documented RAM to NRTI = 50% ; NNRTI = 29%, PI = 39%, INSTI = 2%
  - Reason for switch: DDI = 38%, tolerability = 22%, CV risk reduction = 20%

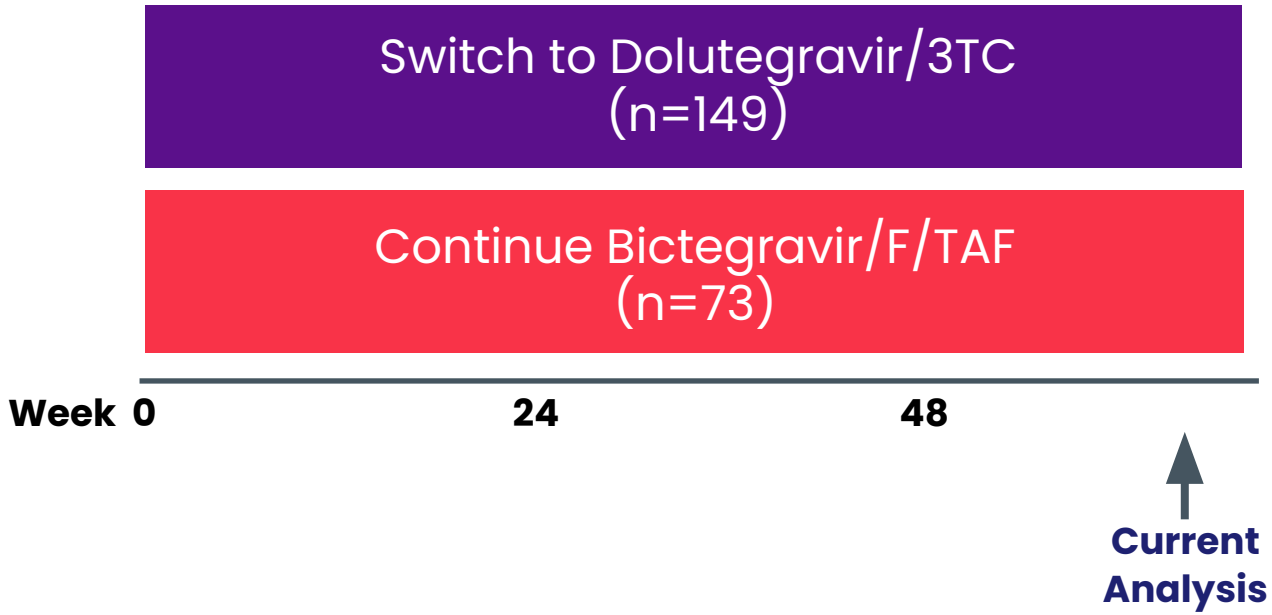
- After median follow-up of 3 years
  - No virologic failure
  - Discontinuation in 13 (12%)
    - Side effects = 5
    - Change to LA therapy = 2
    - Baseline DOR-RAM V106A = 1
    - Low level viremia < 100 c/mL = 2 (switch to DTG/3TC + DOR)

Sammet S et al. AIDS 2024 ; # THPEB095

DYAD Study: **Switch to Dolutegravir/3TC in Virologically Suppressed PWH on Bictegravir/F/TAF**

Phase 4 (single-center cohort)

Open-label, non-inferiority
HIV RNA <50 copies/mL on bictegravir/F/TAF before switch
Key exclusion criteria:
- HBV
- Prior virologic failure
- INSTI resistance
- Severe hepatic impairment



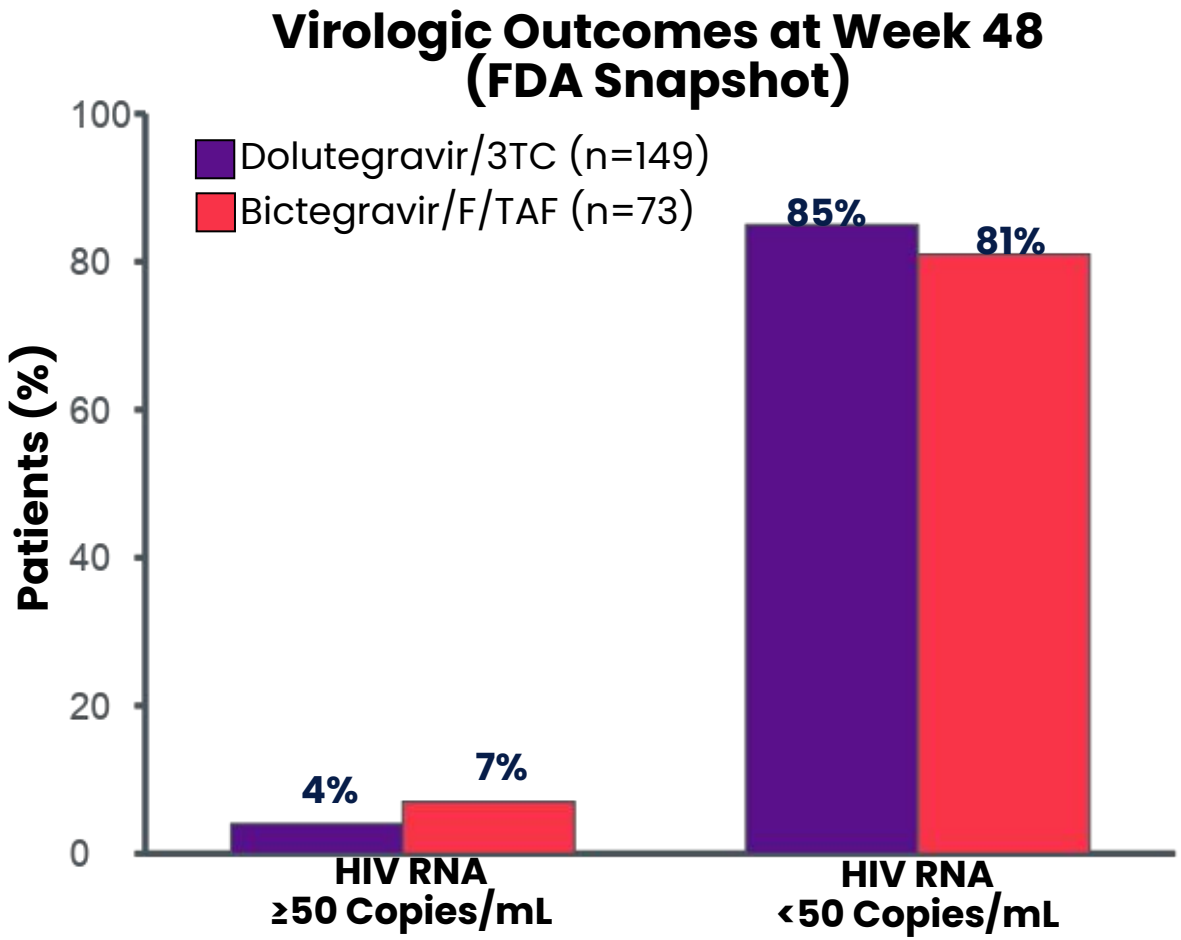
SBR: stable baseline regimen.
Primary outcome:
HIV RNA ≥50 copies/mL at week 48 (FDA snapshot).
Baseline characteristics:
Age (median): 49-51 years.
Male: 86%.
CD4: 720-734 cells/μL.
BMI: 30 kg/m^2.
Baseline resistance mutations:
INSTI/NNRTI/NRTI/PI: 1%/4%/13%/19%.

Rolle CP, et al. IAS 2024. Abstract THPEB089.

DYAD Study: **Switch to Dolutegravir/3TC in Virologically Suppressed PWH on Bictegravir/F/TAF**

- Virologic efficacy following switch to dolutegravir/3TC
  - Non-inferior to continuing bictegravir/F/TAF

- Drug-related adverse events and withdrawals
  - More frequent with dolutegravir/3TC



Rolle CP, et al. IAS 2024. Abstract THPEB089.

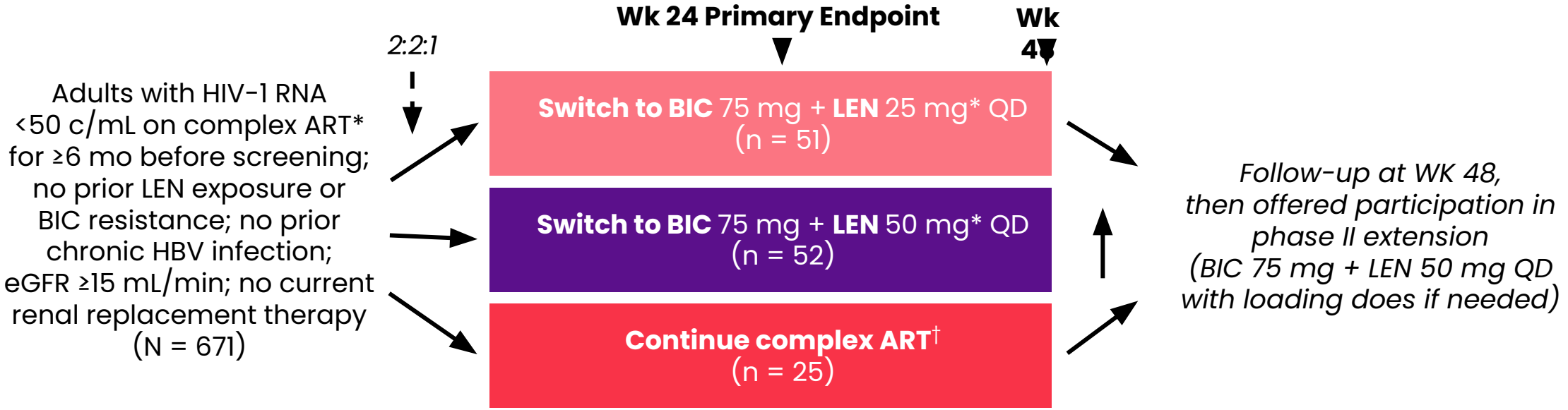
ARTISTRY-1: **Background**

- Gold standard for treating HIV is daily single-tablet regimens[1-3]
  - However, because of comorbidities, drug resistance, toxicities or intolerance, and drug–drug interactions, some people with HIV currently need more complex ART regimens
- Bictegravir + lenacapavir proposed to simplify treatment in people with HIV who are virologically suppressed and ineligible for current single-tablet regimens
  - Bictegravir, guideline-recommended INSTI: high barrier to resistance[1,4]
  - Lenacapavir, HIV-1 capsid inhibitor: no documented de novo resistance before exposure[5]
- Phase II ARTISTRY-1 found that switch from complex ART to bictegravir + lenacapavir was safe and effective in maintaining virologic suppression after 24 wk[6]
  - Current analysis presents 48-wk efficacy and safety from phase II/III ARTISTRY-1[7]

1. clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf.
2. Chang. BMC Infect Dis. 2022;2. 3. Rolle. J Virus Erad. 2020;6:100021. 4. Acosta. Antimicrob Agents Chemother. 2019;63:e02533-18.
5. Dvory-Sobol. Curr Opin HIV AIDS. 2022;17:15. 6. Mounzer. CROI 2024. Abstr 642. 7. Mounzer. AIDS 2024. Abstr OAB2602.

ARTISTRY-1: **Study Design**

- Multicenter, open-label, randomized phase II/III trial



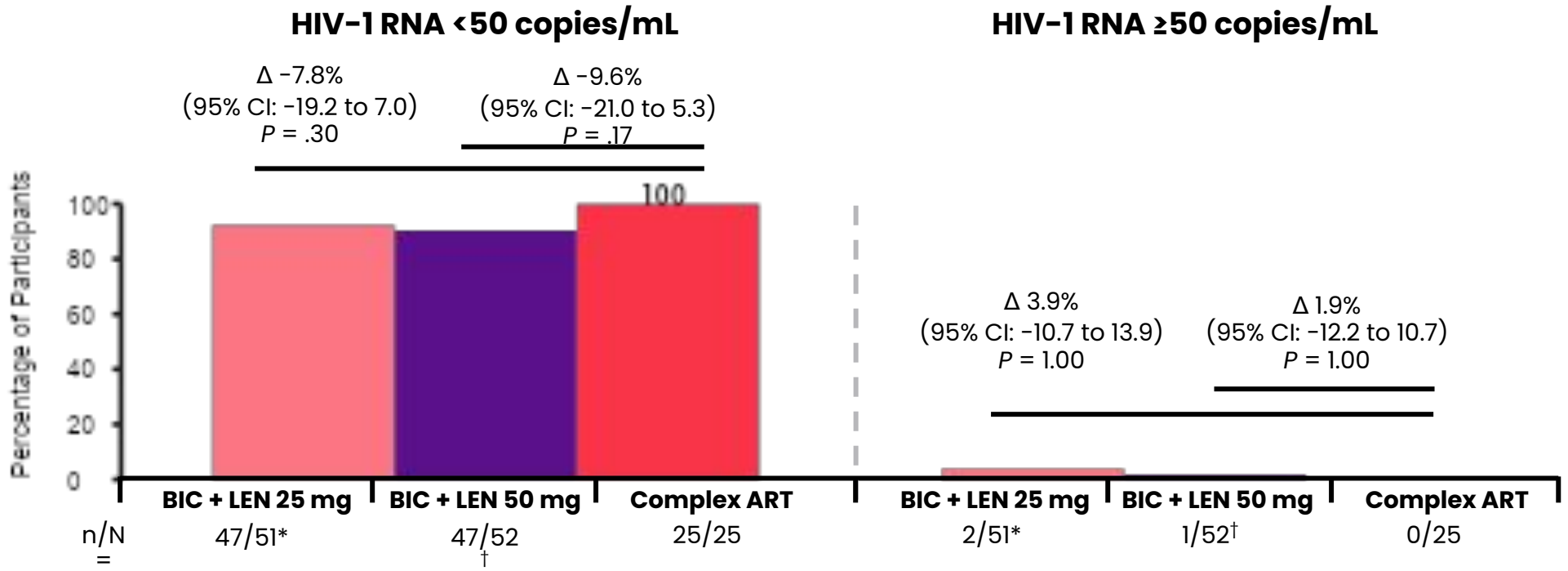
*After LEN 600 mg loading dose on Days 1 and 2.

†Regimens containing boosted PI/NNRTI + ≥1 agent of another class (not NRTI), requiring ≥2 pills/day, dosing administered >1/day, or containing parenteral/oral agents.

- Wk 48 endpoints: proportion with HIV-1 RNA <50 c/mL (FDA Snapshot), safety, CD4+ cell count change from baseline

NCT05502341. Mounzer. AIDS 2024. Abstr OAB2602.

ARTISTRY-1: **Virologic Suppression at Wk 48**



*2 participants discontinued study drug due to toxicity or participant decision (n = 1 each) before Wk 28 visit and did not have virologic data. †4 participants discontinued study drug due to toxicity, death, participant decision, or investigator decision (n = 1 each) before Wk 28 visit and did not have virologic data.

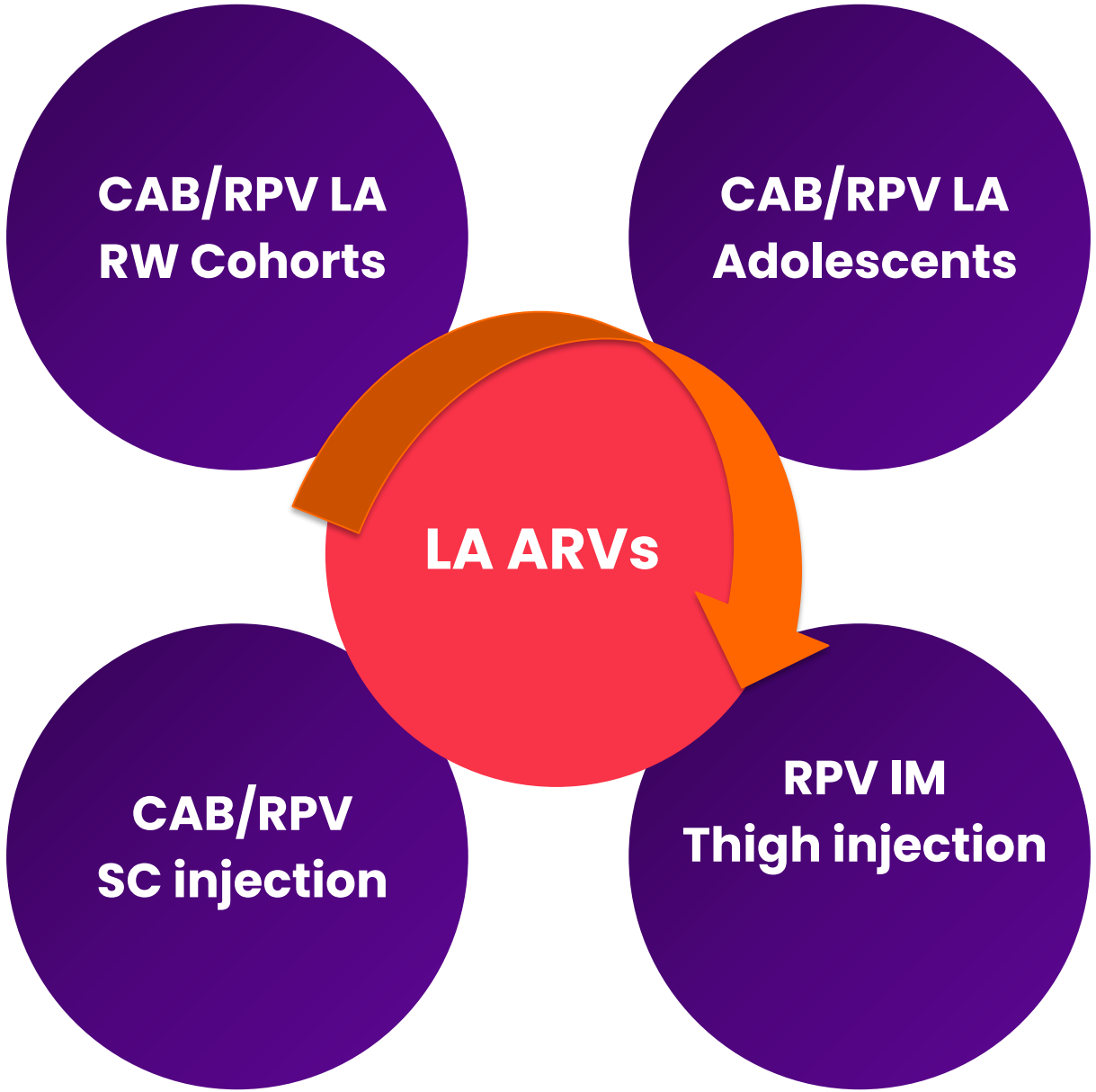
- Virologic suppression rates high across all treatment arms
- CD4+ cell count change and percentage comparable among treatment arms

Mounzer. AIDS 2024. Abstr OAB2602.

ARTISTRY 1: **Investigators' Conclusions**

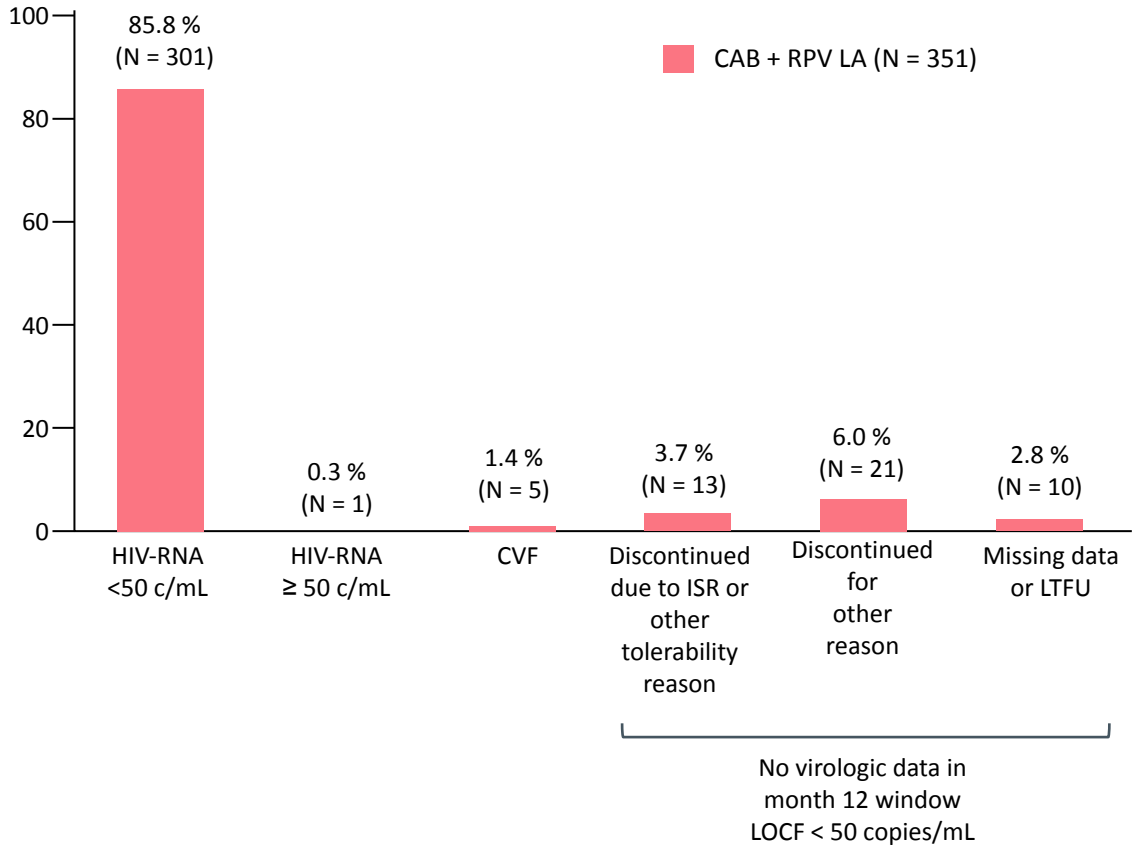
- In people with complex ART regimens, switching to bictegravir + lenacapavir was effective at maintaining viral suppression at 48 wk
  - No significant differences in rates virologic suppression vs continuing complex ART
- Bictegravir + lenacapavir was safe and well tolerated; safety profiles consistent across lenacapavir doses
- Fixed-dose combination bictegravir 75 mg + lenacapavir 50 mg (as a single-tablet regimen) to be evaluated in phase III portion of this study

Mounzer. AIDS 2024. Abstr OAB2602.


CAB/RPV LA
RW Cohorts
CAB/RPV LA
Adolescents
LA ARVs
CAB/RPV
SC injection
RPV IM
Thigh injection

CAB + RPV LA Q2M in real-world: **CARLOS cohort**

- Multicenter, prospective cohort, Germany



Confirmed virologic failures (N = 5)

	NNRTI RAM at failure	INSTI RAM at failure
Case 1	YES	YES
Case 2	NO	NO
Case 3	YES	YES
Case 4	NO	NO
Case 5	YES	NO

None had HIV-subtype A1/A6 or drug-RAM at baseline

Jonsson-Oldenbüttel C, et al. AIDS 2024 ; # TUPEB095

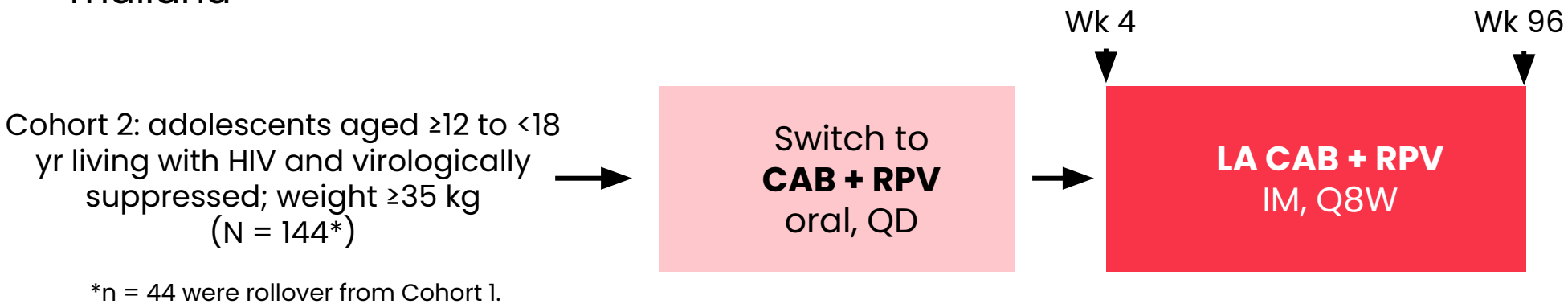
IMPAACT 2017/MOCHA Cohort 2: **Background**

- LA CAB + RPV approved in 2022 for people living with HIV aged ≥12 yr, weighing ≥35 kg, and virologically suppressed on a stable ART regimen[1]
- IMPAACT 2017/MOCHA study network is examining LA CAB + RPV in treatment of adolescents living with HIV[2,3]
  - Cohort 1 results (where adolescents *retained* their background ART) informed approval of LA CAB + RPV in adolescents living with HIV
  - Cohort 2 results (where adolescents *switched* from their background ART) supported efficacy and safety of switch to LA CAB + RPV, with data to Wk 24
- Current study reports cohort 2 safety, efficacy, and PK data in adolescents after switch to LA CAB + RPV, with data to Wk 48[4]

1. Cabotegravir and Rilpivirine PI. 2. Lowenthal. Lancet HIV. 2024;11:e222.
3. Gaur. Lancet HIV. 2024;11:e211. 4. Gaur. AIDS 2024. Abstr OAB2606LB.

IMPAACT 2017/MOCHA Cohort 2: **Study Design**

- Multicenter, open-label, noncomparative phase I/II study of LA CAB + RPV following oral lead-in
  - Cohort 2 enrolled at 18 global sites across US, Uganda, Botswana, South Africa, and Thailand



*n = 44 were rollover from Cohort 1.

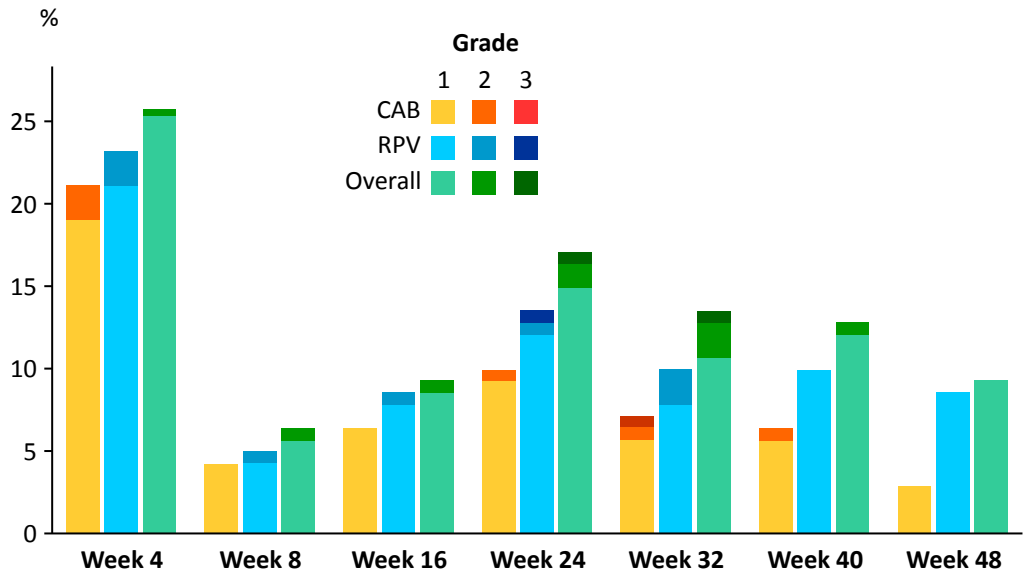
- **Primary outcome**: safety (adverse events, deaths) through Wk 24
- **Key secondary outcomes**: pharmacokinetics, plasma HIV-1 RNA levels, number of participants with virologic failure, and patient satisfaction

Gaur. AIDS 2024. Abstr OAB2606LB. NCT03497676.

LA CAB + RPV IM in adolescents

- IMPACT 2017 Cohort 1: CAB + RPV LA IM (dose similar to adults) Q4W or Q8W in adolescents ≥ 12 years ≥ 35 kg
- 144 adolescents (median age 15 years): at W48, all participants virologically suppressed

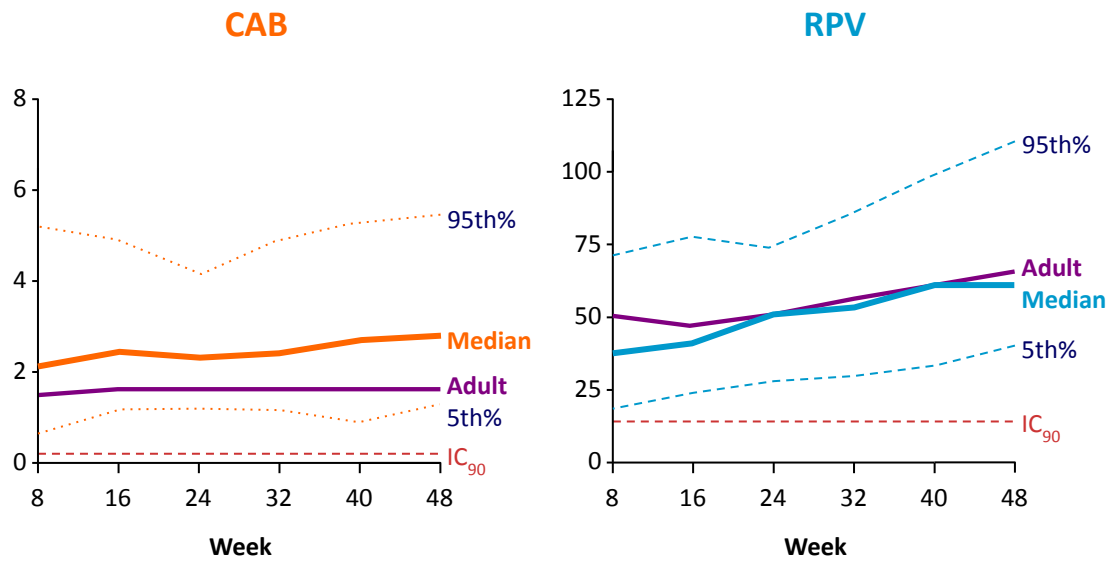
Injection site reactions



Number of participants with injections	142	142	141	141	141	141	140

1 discontinuation at W48

Pharmacokinetics: Trough concentrations (ng/mL)



CAB: 2.77 µg/mL (IQR: 1.99-3.55)
RPV: 67.9 ng/mL (IQR: 52.8-82.4)

Gaur A, et al. AIDS2024 ; # OAB2606LB

IMPAACT 2017/MOCHA Cohort 2: **Virologic Outcomes**

Virologic Suppression

- Virologic suppression maintained in 97.2% (IQR: 93.9-99.2) of participants at Wk 48
  - Defined as HIV-1 RNA <50 copies/mL by FDA Snapshot

Virologic Failure

- No virologic failure in any participants at Wk 48
  - Defined as 2 consecutive HIV-1 RNA measurements ≥200 copies/mL

- No unexpected safety events, no drug-related serious adverse events, no deaths or life-threatening events
- Injection-site reactions: 34%
- Preferred long-acting injectable ART over oral ART: 100%

Gaur. AIDS 2024. Abstr OAB2606LB.

IMPAACT 2017/MOCHA Cohort 2:
Investigator's Conclusions at Wk 48

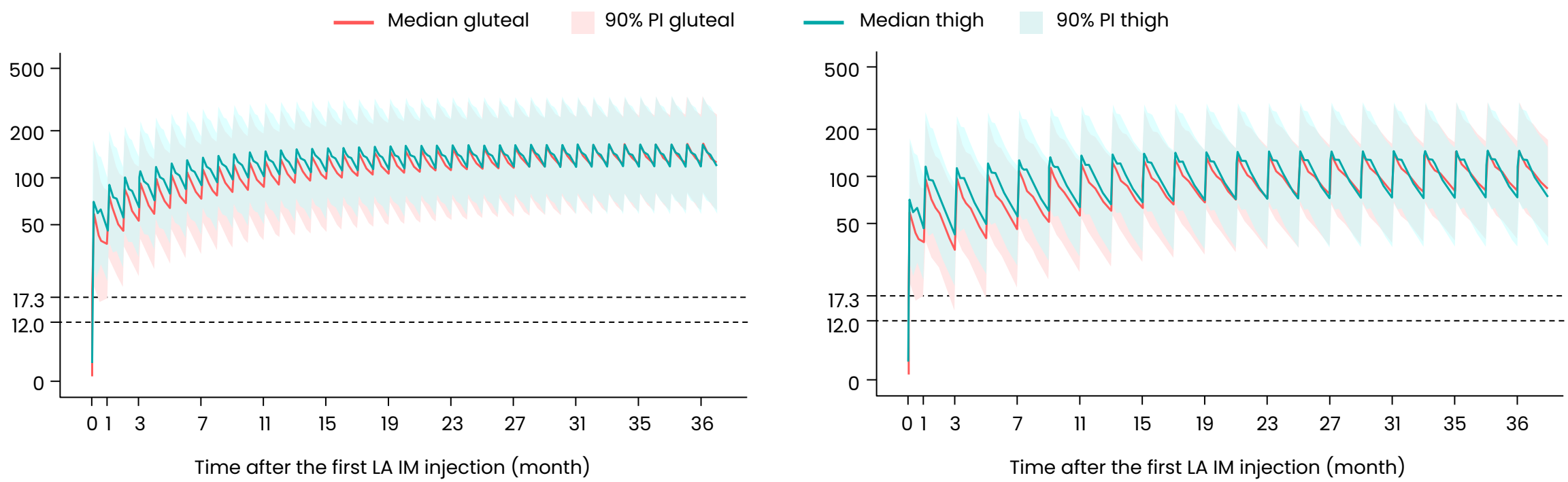
- No new safety signals with use of LA CAB + RPV in adolescents who switched from background ART
- In PK analysis, CAB and RPV troughs were comparable with those previously reported in adults
- Treatment with LA CAB + RPV maintained virologic suppression in 97.2% of participants
- All patients preferred LA CAB + RPV over oral ART
- Data continue to support safety and efficacy of switch to LA CAB + RPV among adolescents living with HIV who are aged ≥12 yr and weigh ≥35 kg
  - Study follow-up ongoing through Wk 96

Gaur. AIDS 2024. Abstr OAB2606LB.

RPV LA IM in thigh: **Population PK**

- 118 PWH + 14 healthy volunteers

RPV plasma concentration (ng/mL)



- **Conclusion:** comparable PK profile after gluteal and thigh IM injections

Dari A, et al. AIDS2024 ; # WEPEB113

FLAIR SC Substudy: **Background**

- LA CAB + RPV FDA approved for monthly or every-2-mo administration via gluteal IM injections by healthcare professional[1-3]
- Phase III FLAIR study demonstrated noninferior efficacy of switching from daily oral therapy to monthly LA CAB + RPV at Wk 48[4]
  - 91% of participants preferred LA injectable option to daily oral option
- Interest in alternate methods of administration, including those that might allow self-administration in home environment
  - Data from healthy volunteers receiving single CAB SC injections support further study[5,6]
- Current FLAIR substudy examined efficacy, safety, tolerability, pharmacokinetics, and patient-reported outcomes in patients with viral suppression after >3 yr of IM injections who switched to SC injections[7]

1. DHHS Guidelines ART 2024. 2. EACS AIDS Guideline v. 11.1. 2022. 3. Ghandi. JAMA. 2023;329:63. 4. Orkin. NEJM. 2020;382:1124. 5. Spreen. JAIDS. 2014;67:481. 56 Spreen. JAIDS. 2014;67:487. 7. D'Amico. AIDS 2024. Abstr OAB2604.

CAB LA IM in thigh:
Population PK simulation

- Simulations demonstrate the potential for chronic thigh injections QM and intermittent thigh injections both QM and Q2M of up to two consecutive thigh injections, but not for chronic Q2M thigh injections

Han K, et al. CROI 2024 ; # 617

FLAIR SC Substudy: **Design**

- Optional substudy of randomized, multicenter, parallel, open-label phase III study

*N = 475; n = 243 originally randomized to LA CAB + RPV; n = 232 originally randomized to DTG/ABC/3TC who switched to LA CAB + RPV in extension phase.
†Formulation, volume, and injection frequency remained the same between IM gluteal injections and SC abdominal injections.

- Primary endpoint: PK parameters after SC abdominal injections vs IM gluteal injections
- Key secondary endpoints: HIV-1 RNA ≥50 c/mL, HIV-1 RNA <50 c/mL, CVF (2 consecutive HIV-1 RNA ≥200 c/mL), safety, treatment acceptance, satisfaction, and preference

D'Amico. AIDS 2024. Abstr OAB2604. NCT02938520.

LA CAB + RPV SC

- Sub-study of FLAIR (CAB + RPV LA Q4M)
- 94 patients on CAB + RPV IM for > 12 months
- Switch to SC injections (D1, W4, W8),
- then back to Q4W IM

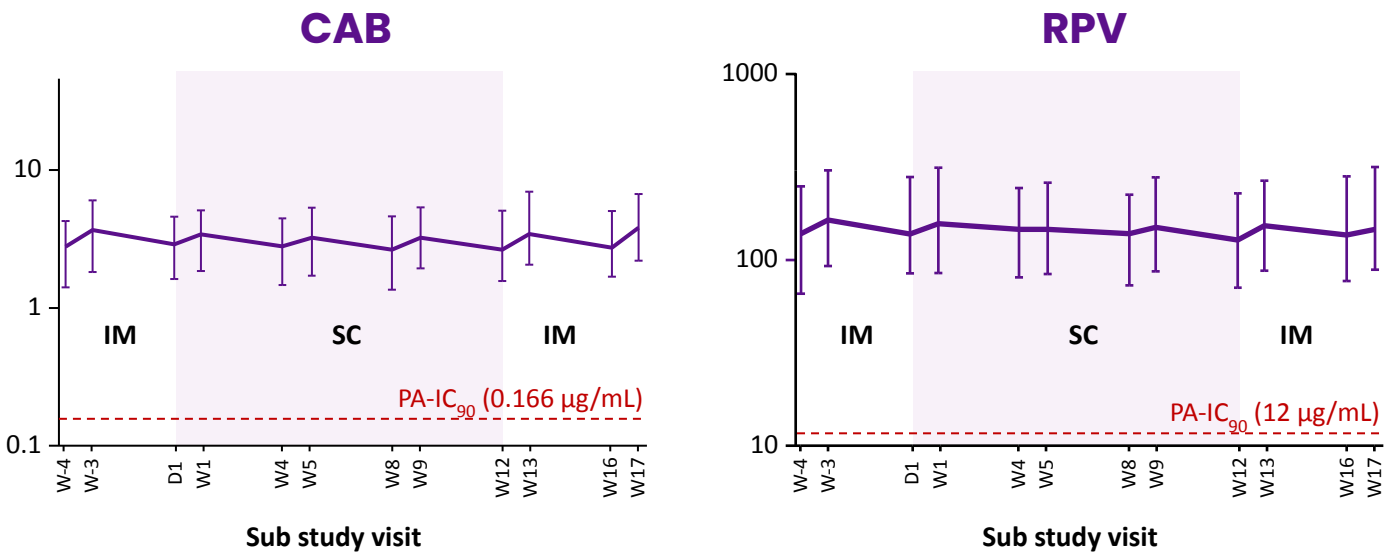
- ISR = 816 events for 542 SC injections
  - Pain 48%
  - Nodules 34%
  - Erythema 26%

- Higher incidence and longer duration of ISRs, lower acceptability and satisfaction vs IM

- Discontinuation for ISR = 5 patients (5%)

- Conclusion: mode of administration not pursued

CAB and RPV plasma concentrations (ng/mL) – Time Plots

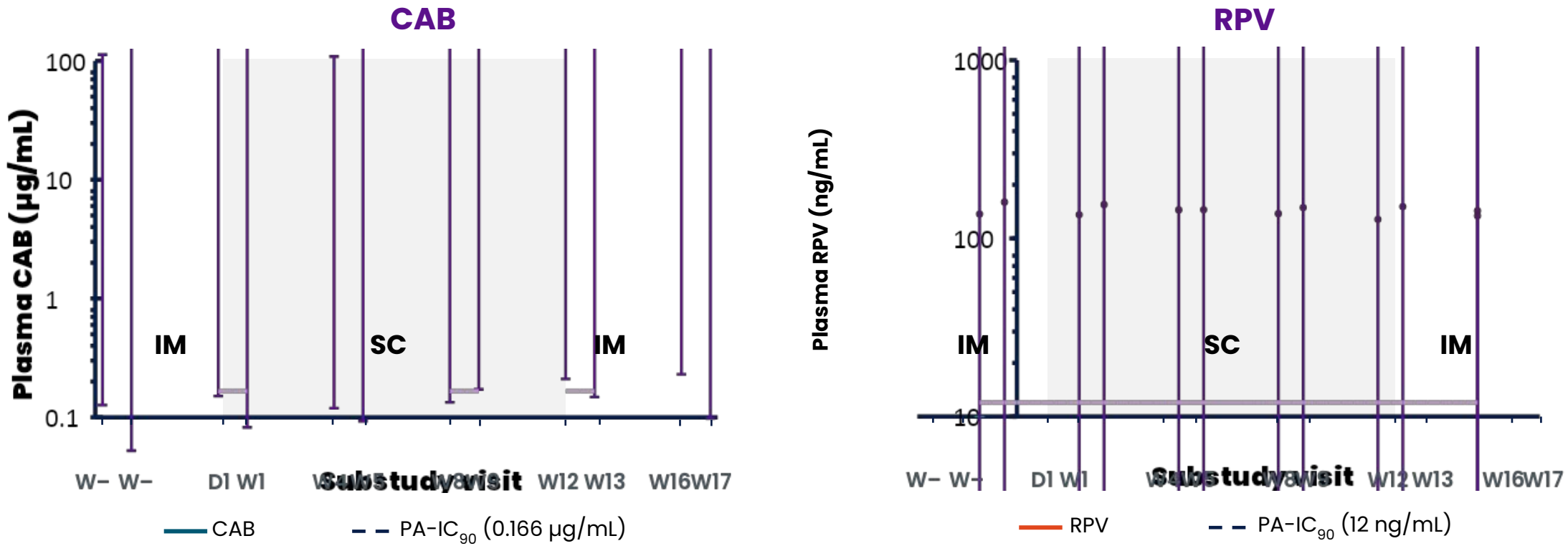


Comparable PK exposures with SC and IM

D'Amico R, et al. AIDS2024 ; # OAB2604

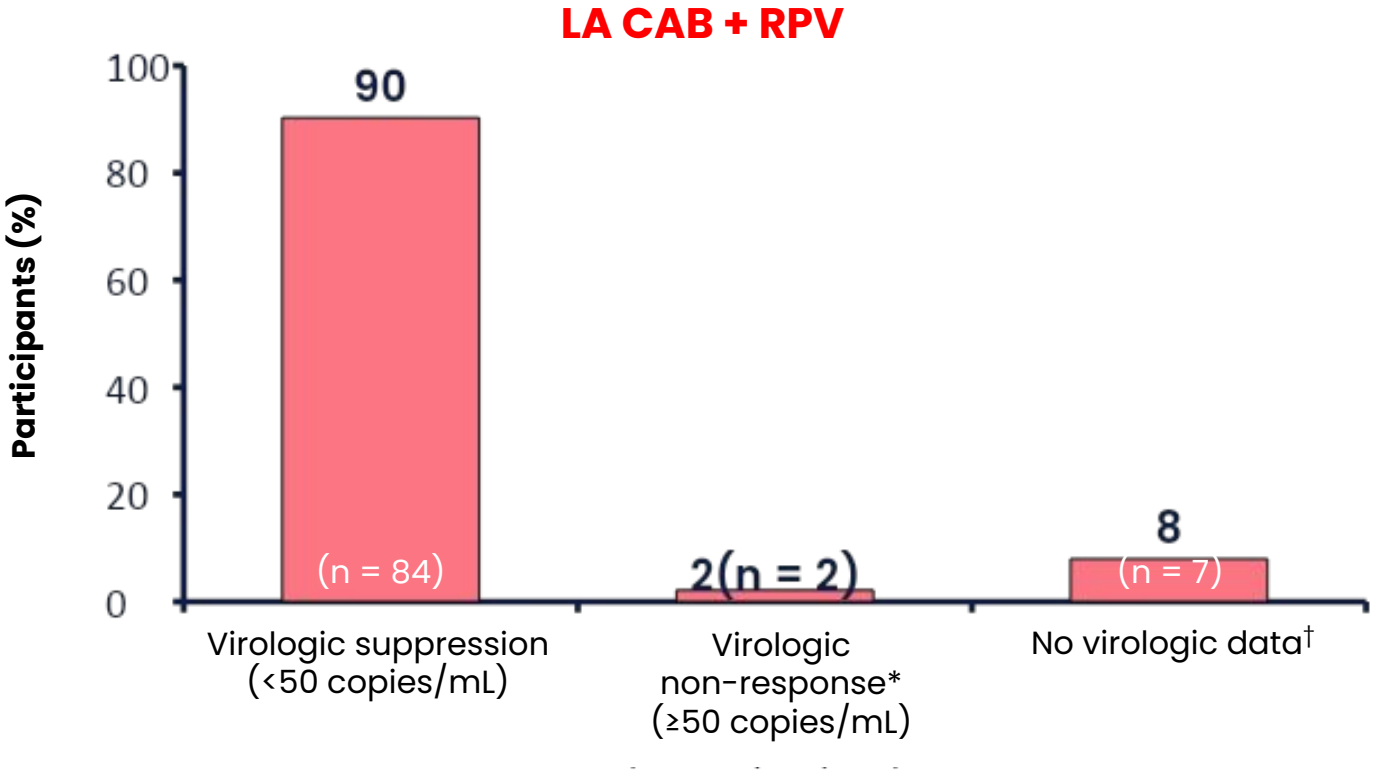
FLAIR SC Substudy: **CAB and RPV Median Concentrations Over Time**

- Median CAB and RPV plasma trough concentrations comparable during SC and IM dosing



D'Amico. AIDS 2024. Abstr OAB2604.

FLAIR SC Substudy:
Virologic Outcomes in SC Phase



- At Wk 12 of SC substudy, 90% of participants had sustained virologic suppression
  - n = 2 with HIV-1 RNA ≥50 copies/mL
- No participants met the criterion for confirmed virologic failure (2 consecutive HIV-1 RNA ≥200 c/mL) during the substudy period

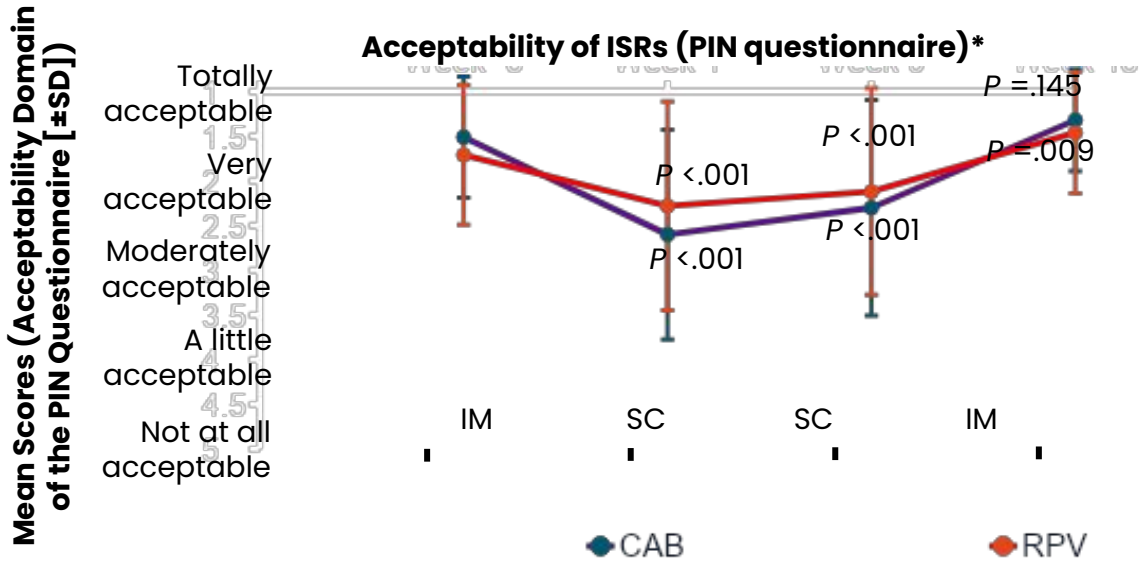
*n = 1 with HIV-1 RNA ≥50 copies/mL at substudy Wk 12; resuppressed by Wk 16, transitioned to commercial LA CAB + RPV at substudy end. n = 1 with HIV-1 RNA ≥50 copies/mL at substudy Wk 8, 12, and 16; transitioned to DRV/COBI/FTC/TAF at substudy end.

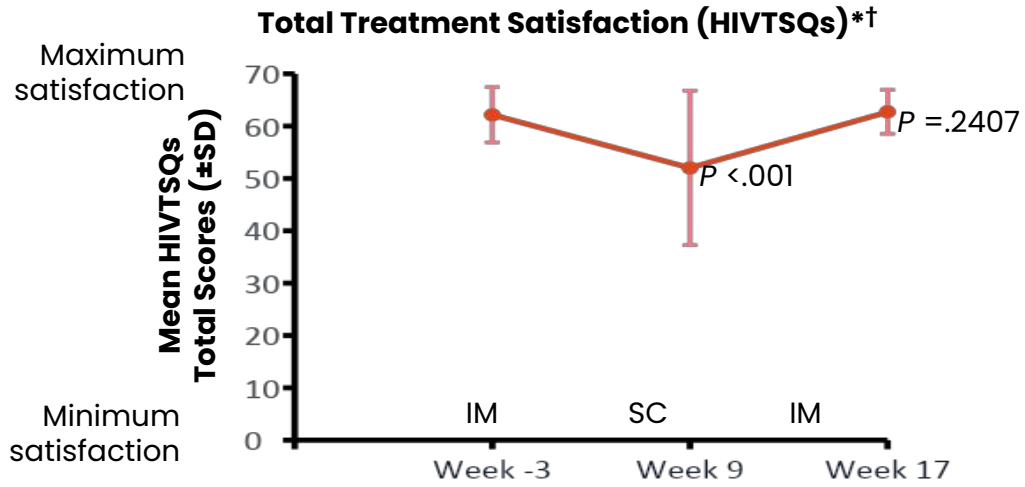
†n = 2, discontinued due to AE; n = 4, discontinued for other reasons (n = 2, protocol deviation; n = 2 participant withdrawal); n = 1, on study but missing data in window.

D'Amico. AIDS 2024. Abstr OAB2604.

FLAIR SC Substudy: **Patient Satisfaction**

- Statistically lower acceptance and treatment satisfaction scores with **SC** vs **IM**
  - Reflects high percentage of pain, nodule, and erythema ISR events with SC, and high overall treatment satisfaction with IM
- 1 wk post third SC injection, **59% (n = 50/85) preferred IM** vs **34% (n = 29/85) preferred SC**
  - **Common reasons to prefer IM:** less injection-site swelling, 58% (29/50); fewer nodules, 58% (29/50), less pain, 54% (27/50)
  - **Common reasons to prefer SC:** convenience, 86% (25/29); injections not interfering with daily activities, 59% (17/29)





D'Amico. AIDS 2024. Abstr OAB2604.

FLAIR SC Substudy:
Investigators' Conclusions

- In FLAIR substudy of 12 wk of **abdominal SC administration** of LA CAB and RPV,
  CAB and RPV PK parameters were similar to those with **IM gluteal injections**
  - HIV-1 RNA <50 copies/mL maintained in 90% of participants
- SC injections associated with **high incidence and longer duration of ISRs**
  - Frequency and intensity of IRSs resulted in significantly lower acceptability of/satisfaction with SC administration vs IM administration
  - Most participants (59%) preferred IM injections over SC injections
  - Manufacturer reports no intentions for further development SC self-administration of this regimen

D'Amico. AIDS 2024. Abstr OAB2604.

Injectable CAB LA during pregnancy

- HPTN084 open label extension: Pregnant women could consent to continue receiving CAB-LA injections during pregnancy

- 367 pregnancies during follow-up (12/100 PY)
  - Maternal, pregnancy and infant outcomes: similar compared to women with CAB only prior to pregnancy and with no CAB (TDF/FTC)

- PK sub-study in 75 pregnant women (data for the first 50)
  - CAB-LA $C_{through}$ decline from the 1st to 3rd trimester and are lowest in 3rd trimester
  - CAB-LA $C_{through}$ > 4 x PA-IC_{90} in 100% at 1st and 2nd trimester, 98% at 3rd trimester
  - Conclusion: dose modifications not recommended if CAB-LA continued during pregnancy

Delany-Moretlwe S, et al. AIDS2024 ; # SY2503 ; Marzinke M, et al. AIDS 2024 ; # SY2504

HIV RNA screening in persons on CAB-LA PrEP: **risk of false positive**

- HPT083 open label extension study
  - 27 335 visits in 2 620 participants, with HIV RNA testing at each visit at local lab
  - 29 acquired HIV infection during follow-up
    - in 5/29, HIV infection first identified by an isolated positive RNA test (median VL 1597 c/mL, range: 124 to 4120)
    - the 24 others had Ag/Ab rapid testing positive in addition to positive PCR
  - 22 participants had a single isolated positive RNA test = False positive (median VL BLQ, range : BLQ to 149)

Performance of isolate positive RNA result

	PPV	False positive rate	Sensitivity
Overall	18.5%	0.08%	96.4%
CAB-LA visits within last 6 months	9.1%	0.09%	87.5%
No CAB-LA visits within the last 6 months	60%	0.06%	100%

- Conclusion
  - Poor performance for detecting HIV infection with CAB LA PrEP of isolated positive RNA result
  - Most single isolated positive RNA results are false positive
  - Although infrequent, might complicate clinical management

Landovitz R, et al. AIDS 2024, # OAE0406LB

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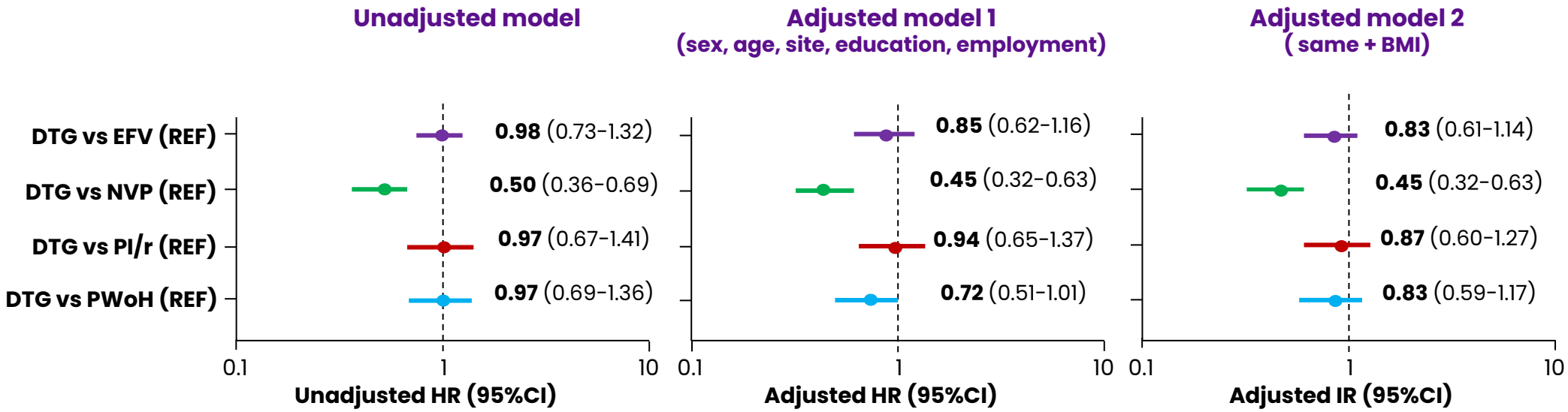
Riesgo CV

DTG and incident hypertension

- Prospective cohort Kenya, Nigeria, Tanzania and Uganda
- 2477 PWH and 455 without HIV followed for a median of 5.4 years (incidence of hypertension: 14%)
- Hypertension ≥ 140/90 mm Hg at 2 consecutive 6-monthly visits or receipt of anti-hypertensive drug

Unadjusted and adjusted models examining associations between time-varying ART and incident hypertension



- Conclusion: DTG not associated with increased incidence of hypertension

Romo M, et al. AIDS2024 ; # OAB3404

REPRIEVE Trial: **Abacavir Exposure Status and Risk of Cardiovascular Events**

Phase 3

PWH on stable ART
40 to 75 years of age
Low-to-moderate risk atherosclerotic CVD
No statin use in past 9- days

Pitavastatin (n=3888)

Placebo (n=3881)

36% Reduction in MACE With Pitavastatin Versus Placebo

Current Analysis
Risk of MACE With Prior or Current Exposure to Abacavir

Baseline Characteristics (abacavir versus no abacavir exposure)

Age: 52 versus 49 years.
Male: 76% versus 67%.
HIV RNA <LLQ-400 copies/mL: 87% versus 88%.
CD4: 617 versus 622 cells/µL.
ASCVD risk score: 5.4% versus 4.2%.
Fasting LDL-C: 109 versus 106 mg/dL.

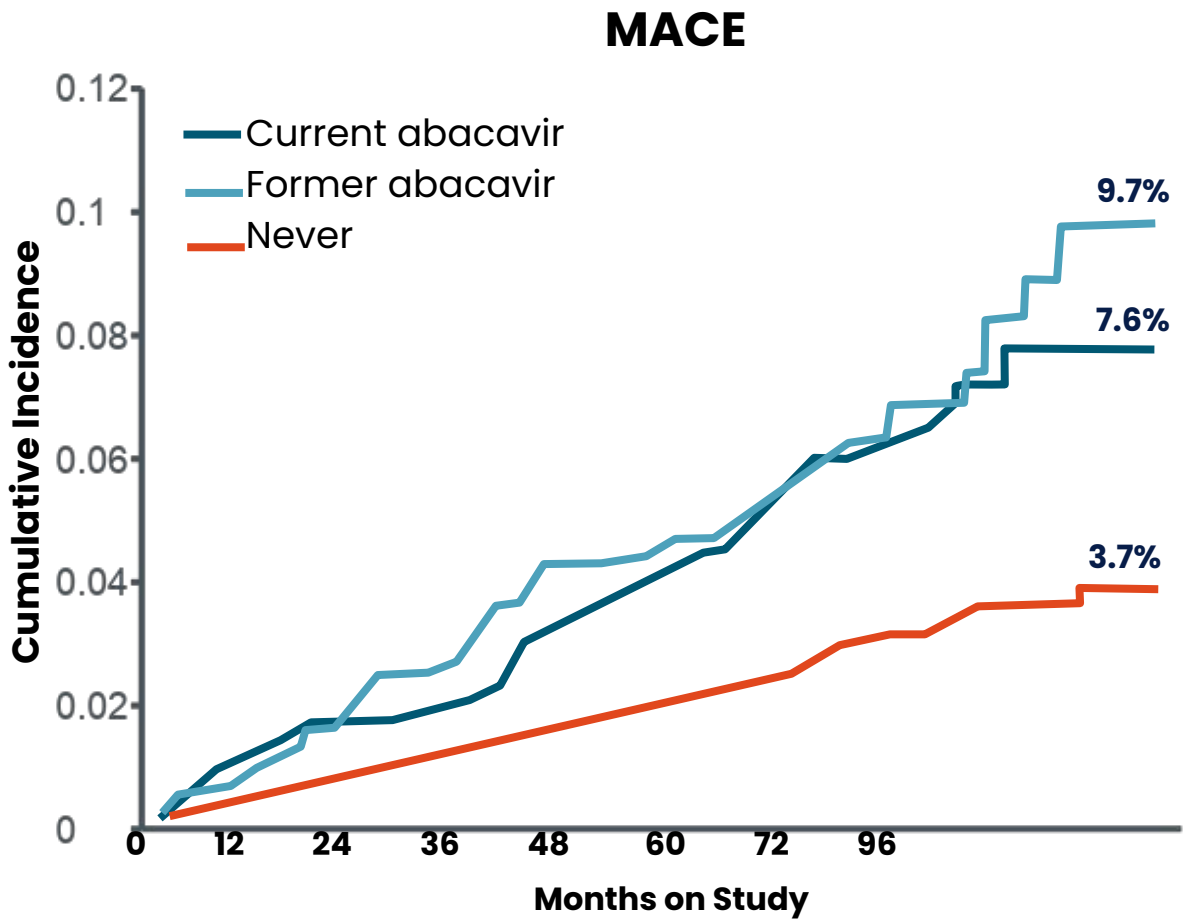
Abacavir exposure: 22%
Former: 9% (3.0 years)
Current: 13% (1.5 years)
No prior abacavir: 78%

REPRIEVE: Randomized Trial to Prevent Vascular Events in HIV.
Median baseline values.

Fichtenbaum CJ, et al. AIDS 2024. OAB3406LB
Grinspoon SK, et al. N Engl J Med. 2023;389:687-699.

REPRIEVE Trial: **Abacavir Exposure Status and Risk of Cardiovascular Events**

- Abacavir exposure (versus none) was associated with higher incidence of MACE (RF-adjusted HR [95% CI])
  - Former: 1.50 (1.04, 2.15)
  - Current: 1.42 (1.00, 2.00)
- Current and former use of tenofovir, PI, and thymidine analogs were not associated with subsequent MACE



MACE: major adverse cardiovascular event.

Fichtenbaum CJ, et al. AIDS 2024. OAB3406LB

REPRIEVE: **ABC Exposure and MACE**

Outcome	Events, n	Participants, n	Unadjusted HR (95% CI)	RF-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)

*Adjusted model components: age, natal sex, race, global burden of disease region, family history of CVD, smoking, hypertension, BMI, substance use, nadir CD4, HIV-1 RNA, entry baseline ART regimen class, creatinine clearance, fasting glucose and lipids.

- INSTIs, NNRTIs or PIs did not appear to change the effects of ABC on MACE
- No association of prior or current use of tenofovir, protease inhibitors, or thymidine analogs with MACE

Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

REPRIEVE: **Investigators' Conclusions**

- At baseline, REPRIEVE ITT population of people with HIV had no prior CVD and low to moderate risk of ASCVD
  - 4.2% median CVD risk score among participants with no ABC exposure
  - 5.4% median CVD risk score among participants with ABC exposure
- After median 5.6 yr of follow-up, current and former use of **ABC associated with higher incidence of subsequent MACE**
  - Independently adjudicated CV endpoints
- Use of tenofovir, protease inhibitors, and thymidine analogs (current and former) not associated with MACE

Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

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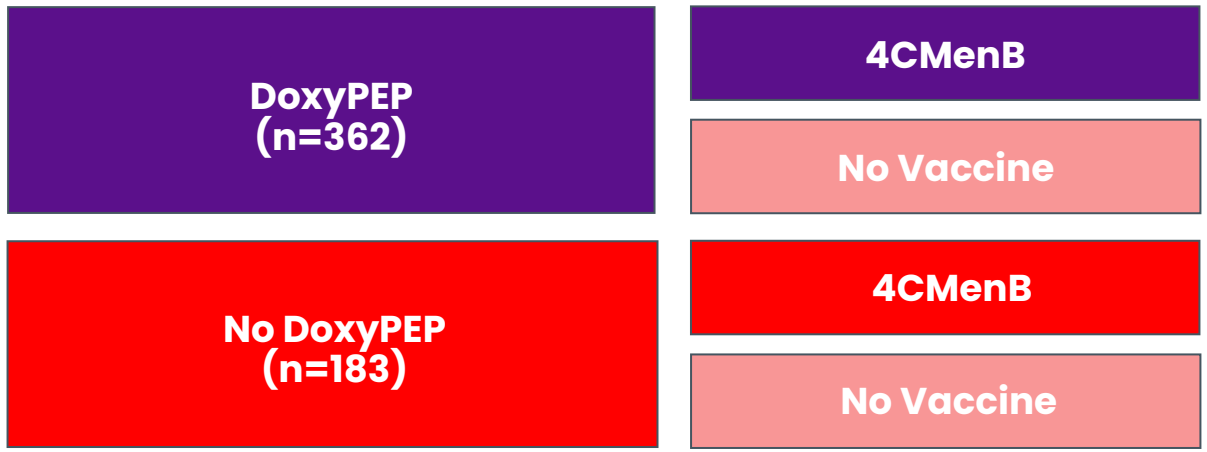
ITS:
PEP y PrEP

DOXYVAC Study:
Prevention of STIs in MSM on PrEP

Phase 3

Open-label, superiority
MSM on PrEP for ≥6 months
Bacterial STI in prior 12 months
No STI symptoms



Up to 96 Weeks Follow-Up

Relative Risk Reduction of STI Incidence (DoxyPEP versus noPEP arm)

Syphilis: 79%
Chlamydia: 86%
Gonorrhea: 33%

DoxyPEP: 200 mg within 72 hours of condomless sex.
4CMenB: Meningococcal type B vaccine.
STI testing: baseline and every 3 months.
GC: gonorrhea; CT: Chlamydia trachomatis.
Primary endpoints:
DoxyPEP: incidence of 1st episode of CT or syphilis.
4CMenB: incidence of a 1st episode of GC, 1 month after the second injection.

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

DOXYVAC Study:
Results of the Resistance Analysis

- There was no impact of DoxyPEP on ceftriaxone, ciprofloxacin, and azithromycin susceptibility
- All GC isolates were resistant to tetracycline but the rate of high-level resistance was higher in the DoxyPEP arm
- Monitoring the emergence of 3rd generation cephalosporin resistant isolates remains critical

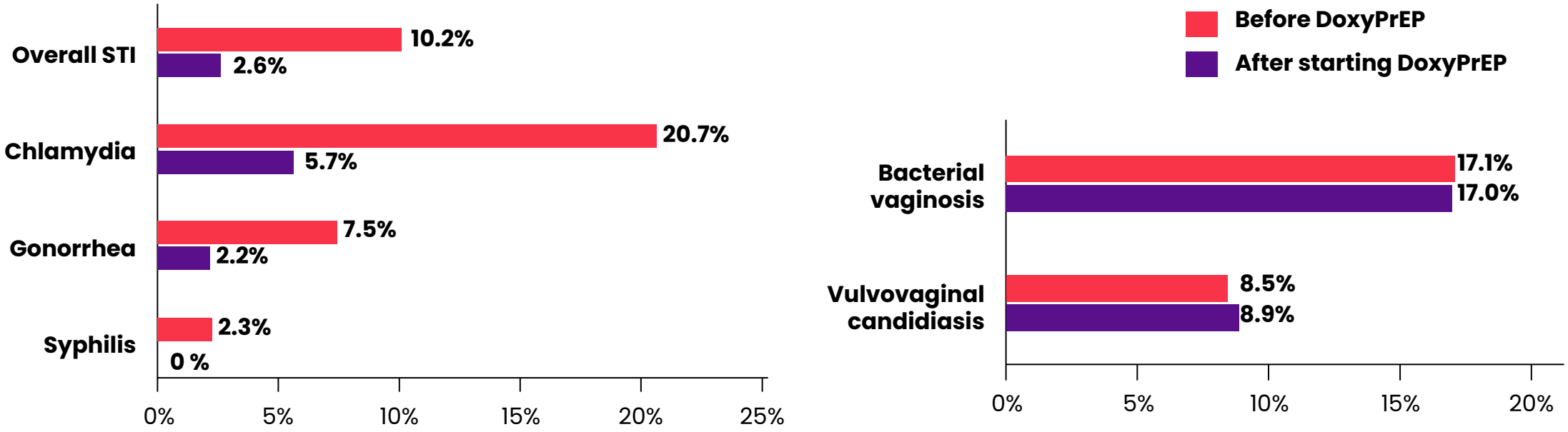
GC: Neisseria gonorrhea.

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

DoxyPrEP in female sex workers

- Retrospective, single-center study, Tokyo
- 40 female sex workers who initiated doxycycline 100 mg/day for STI prevention
- Testing for STI, bacterial vaginosis and vulvovaginal candidiasis every 1-3 months

Incidence (test positivity rate)



- Conclusion: significant decrease of STIs without increase of other vaginal infections

Abe S, et al. AIDS2024 ; # OAC0803

DoxyPrEP in MSM

- Randomized clinical trial double-blind placebo-controlled study, Toronto and Vancouver
- 52 MSM randomized 1:1 to doxycycline 100 mg daily or placebo, for 48 weeks
- STI multi-site screen every 3 months

Bacterial STI incidence at 48 weeks

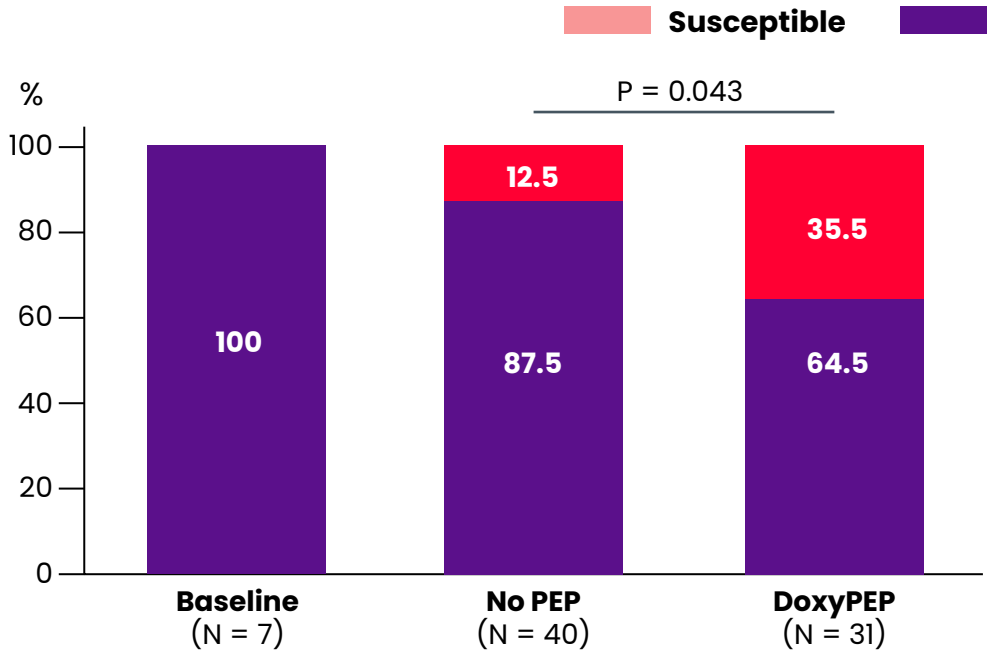
	Total STI		Incidence ratio, per 100 PY		Rate ratio (95% CI)	p
Overall	DoxyPrEP	Placebo	DoxyPrEP	Placebo		
TOTAL	6	31	23.71	119.44	0.20 (0.08-0.51)	< 0.001
Syphilis	1	5	3.95	19.26	0.21 (0.04-0.97)	0.04
Chlamydia	1	13	3.97	50.09	0.08 (0.01-0.49)	0.01
Gonorrhea	4	13	15.88	50.09	0.32 (0.12-0.86)	0.02

Grennan T, et al. AIDS 2024 ; # LB11

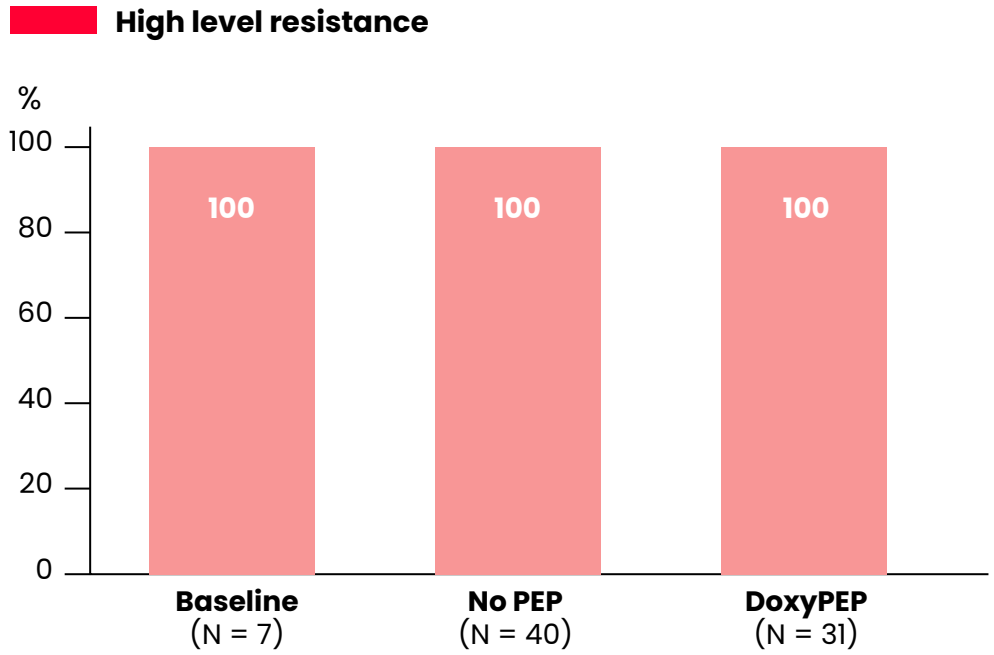
Antimicrobial resistance of Neisseria gonorrhoeae on doxyPEP

- DOXYVAC: prevention of STI in MSM on PrEP (Molina JM, Lancet Infect Dis. 2024 May 23)
- Doxycycline vs no doxycycline 200 mg within 72h post-sex: 80% risk reduction of chlamydia and syphilis

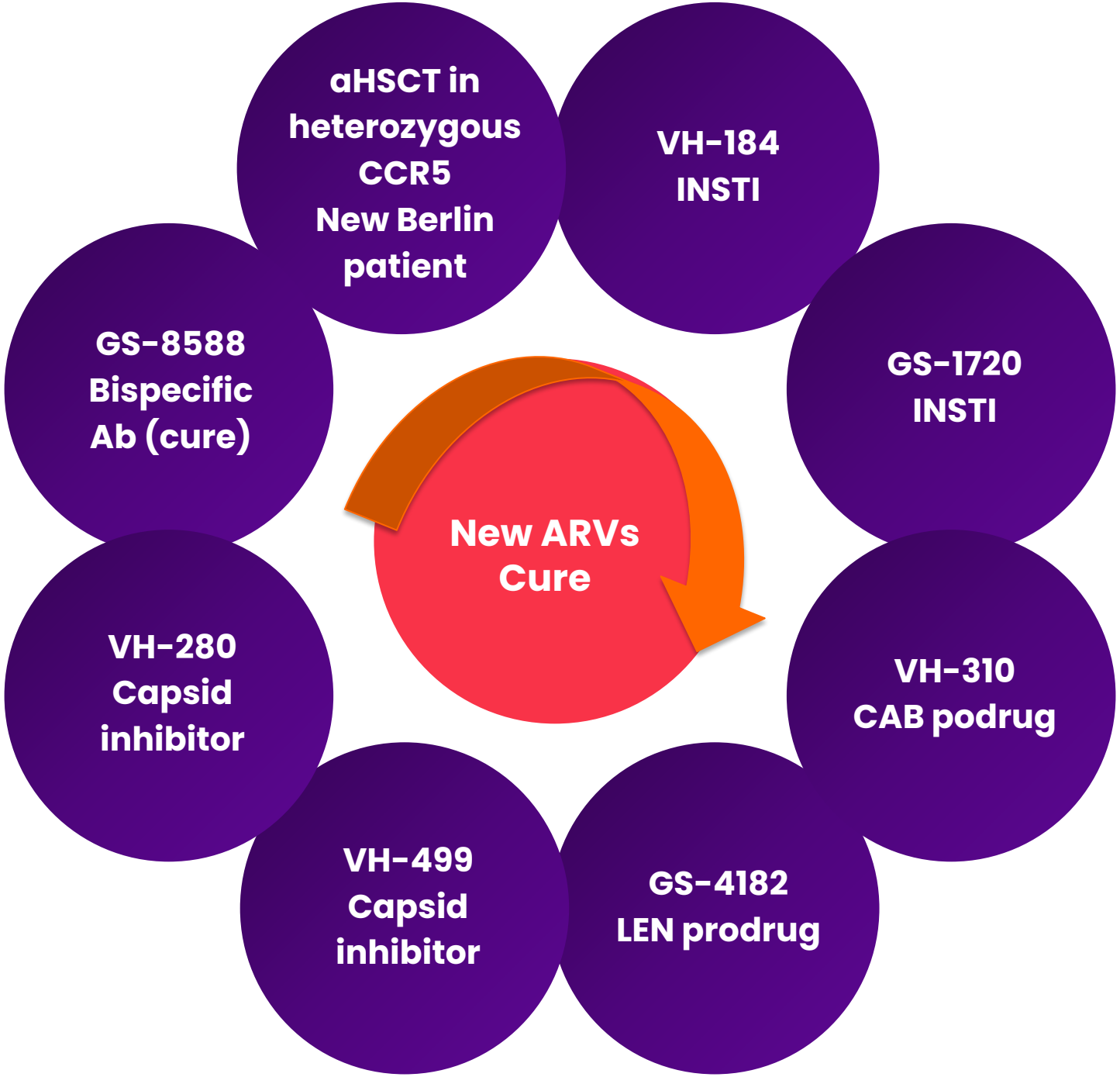
Resistance to tetracycline



Resistance to ceftriaxone



Berçot B, et al. AIDS 2024 ; # SS0404LB


aHSCT in heterozygous CCR5 New Berlin patient
VH-184 INSTI
GS-8588 Bispecific Ab (cure)
GS-1720 INSTI
New ARVs Cure
VH-280 Capsid inhibitor
VH-310 CAB podrug
VH-499 Capsid inhibitor
GS-4182 LEN prodrug

The Next Berlin Patient

While male

- HIV diagnosed 2009 (genotype CCR5 WT/delta 32)
- No ART until 4/2015, then raltegravir + ABC/3TC
- AML diagnosis 4/2015
  - aHSCT 10/2015 from CCR5 WT/delta 32 donor
  - Reduced intensity conditioning

ART interrupted 2018

HIV remission >5.5 years

- No detectable HIV DNA or viral outgrowth post-aHSCT
- Waning HIV-specific antibody and T cell immunity post-aHSCT

AML: acute myeloid leukemia.
aHSCT: autologous hematopoietic stem cell transplantation

Gaebler, et al. IAS 2024. Abstract SS0402LB.

A new case of HIV remission («cure»?) after stem cell transplantation

Cases of HIV long remission after stem cell transplant

Case	Reported year	Type of SCT	Type of malignancy	CCR5 mutation profile	Time on HIV remission	Comments
Berlin patient	2008	aHSCT	Acute myeloid leukemia	homozygous	14 years	Died (recurrent leukemia)
London patient	2019	aHSCT	Hodgkin disease	homozygous	7 years	
Düsseldorf patient	2019	aHSCT	Acute myeloid leukemia	homozygous	5.5 years	Prolonged used of ART before interruption
New-York patient	2022	hBCT	Acute myeloid leukemia	homozygous (2 donors)	3.5 years	
City of Hope patient	2022	aHSCT	Acute myeloid leukemia	homozygous	3 years	63y old and CD4<100 at time of transplant
Geneva patient	2023	aHSCT	Extramedullary myeloid tumor	No mutation (wild type)	3 years	Ruxolitinib for GHVD (impact on HIV reservoir ?)
New Berlin patient	2024	aHSCT	Acute myeloid leukemia	heterozygous	5.5 years	

aHSCT = allogenic hematopoietic stem cell transplant ; hCBT = hap to cord blood transplant

Gaebler C, et al AIDS2024 ; # SS0402LB

Muchas gracias

Esta actividad es posible gracias al apoyo de