CROI 2025: What happened in HIV/STI prevention, and things you need to know!

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AETC MidAtlantic

The MidAtlantic AIDS Education and Training Center (MAAETC)

provides HIV/AIDS education, consultation, technical assistance, and resource materials to healthcare professionals throughout Pennsylvania, Maryland, Virginia, West Virginia, Delaware, and the District of Columbia.

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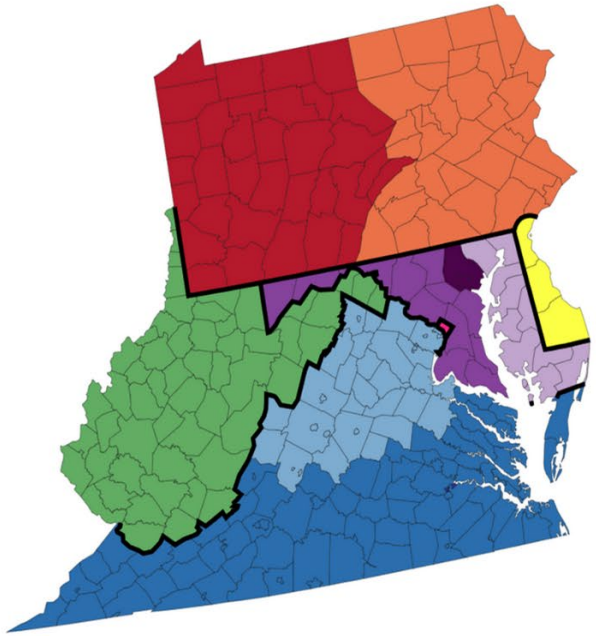

Topics Include:

- HIV Prevention
- HIV Care & Treatment
- HIV & Substance Use
- HIV & Mental Health
- Trauma-Informed Care
- Cultural Humility
- Patient-Centered Care
- Retention & Engagement

High-Quality Education & Training Programs For:

- Physicians, Physicians, & Physician Assistants
- Nurses & Nurse Practitioners
- Dentists & Dental Hygienists
- Patient Educators & Community Health Workers
- Case Managers & Social Workers
- First Responders & EMS Personnel
- Public Health Professionals
- All Members of Interdisciplinary Care Teams

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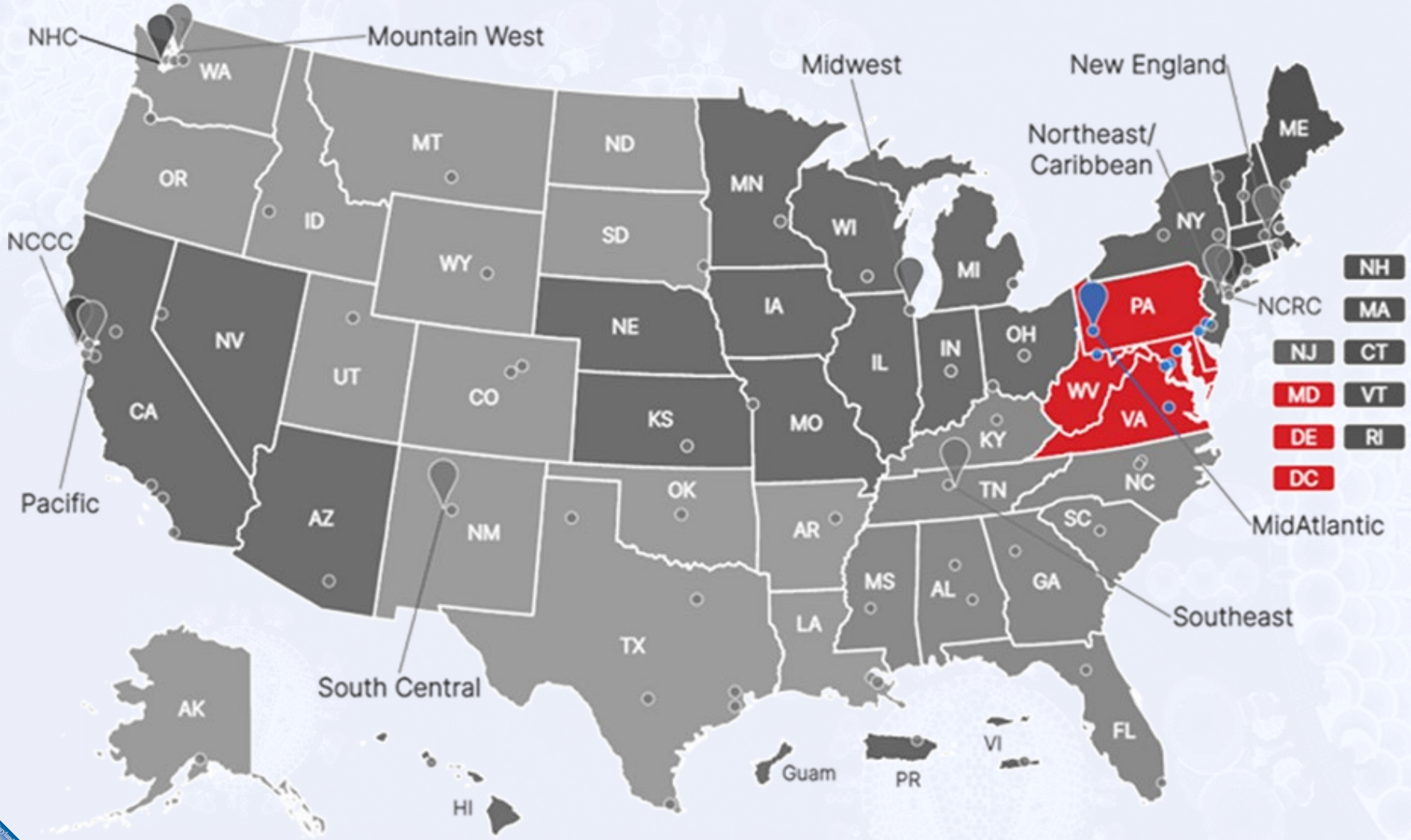

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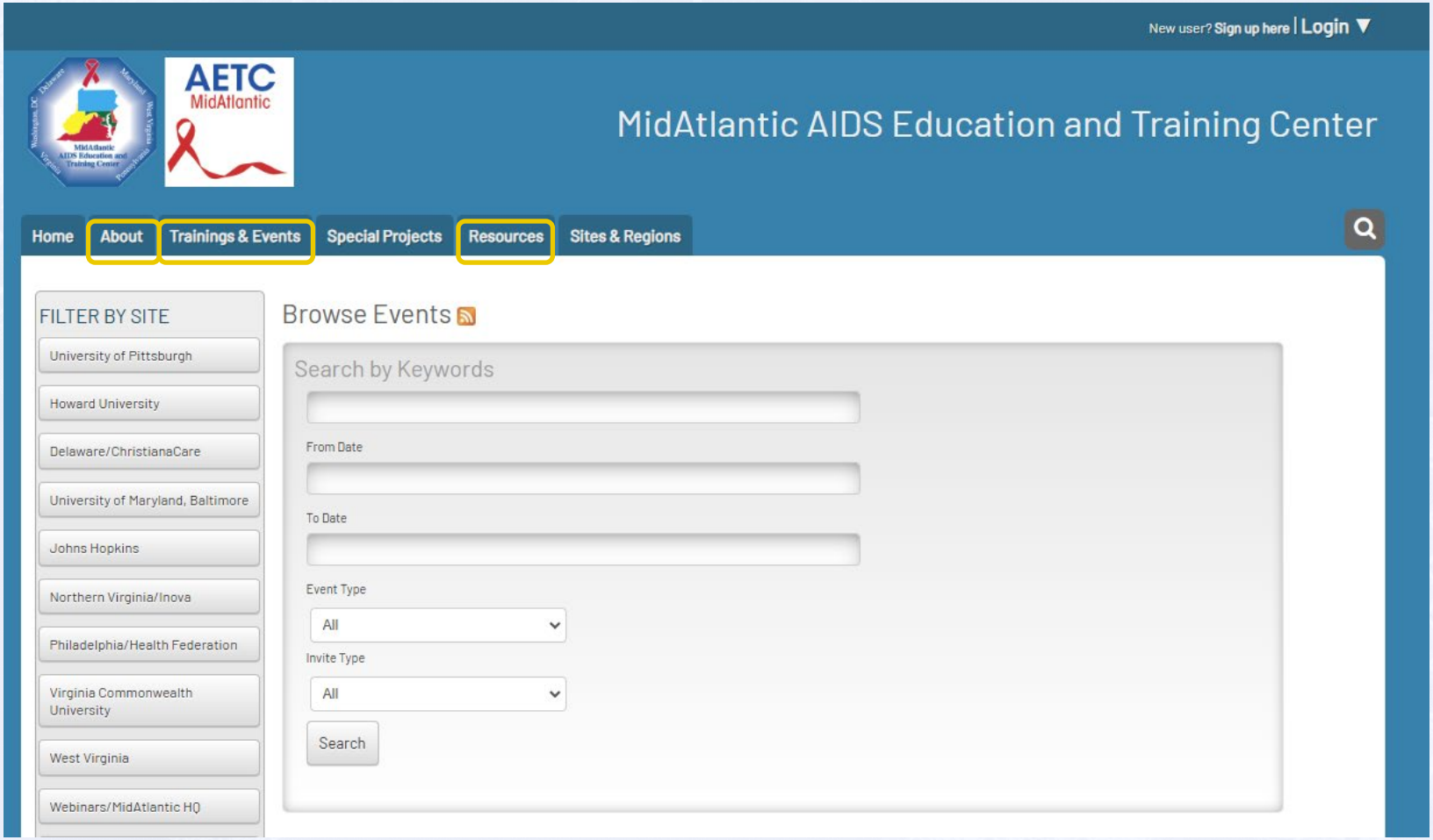
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- The staff and faculty involved with the planning of today's event **do not** have any conflicts of interest to disclose.
- David E. Koren: Speaker (Gilead Sciences and ViiV Healthcare), Independent Consultant (Merck & Co)

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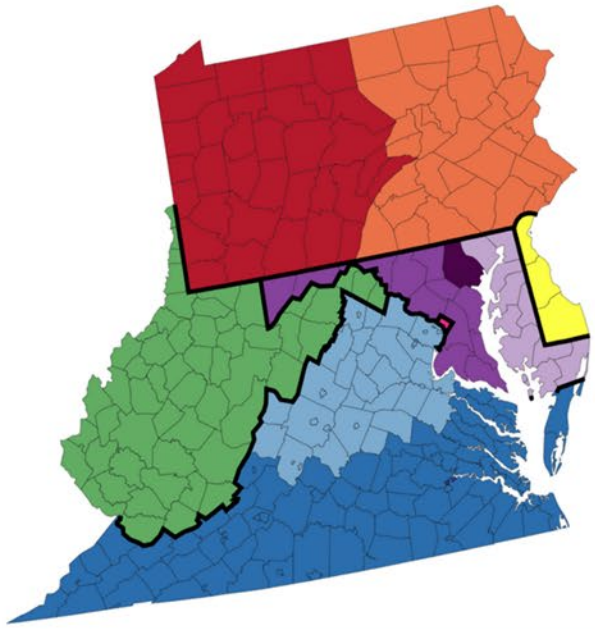

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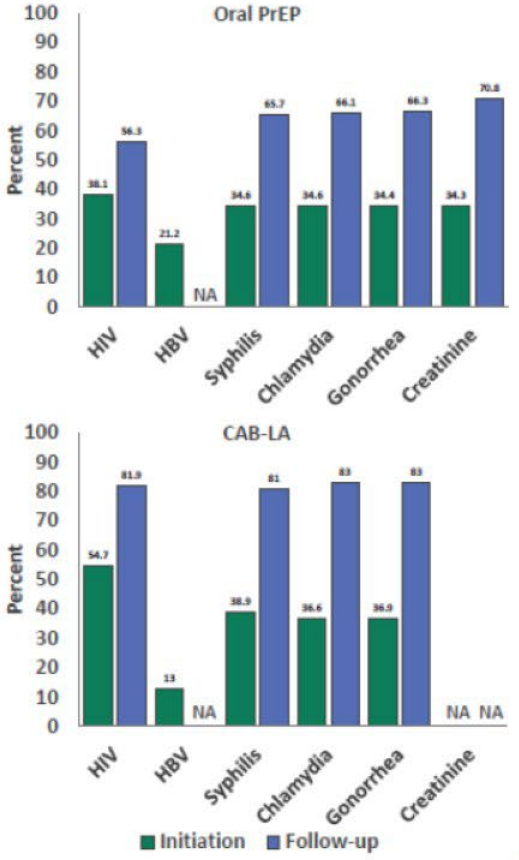
Today's Objectives

- **Review recent updates for HIV prevention from CROI 2025 which can be implemented immediately.**
- **Review recent updates for STI prevention from CROI 2025 which can be implemented immediately.**
- **Discuss recent data regarding antiretroviral agents under development for HIV prevention**

HIV PREVENTION

Suboptimal laboratory testing of PrEP users, US 2022-2023

- For PrEP users, CDC recommends:
  - HIV laboratory-based testing at initiation and follow-up visits
  - STI testing at initiation and follow-up visits
  - HBV testing at initiation
  - Creatinine testing for oral PrEP users
- Evaluated MarketScan database for those starting oral PrEP or CAB-LA in 2022-2023
- >35,000 oral PrEP users, with >12,000 with follow-up prescription
  - Only 38% had lab-based HIV testing at initiation; only 56% at follow-up
- 453 CAB-LA PrEP users, 370 with follow-up prescription
  - Only 55% had lab-based HIV testing at initiation; 82% at follow-up
- Also sub-optimal testing for STIs at initiation



Hoover et al, Abstract 1216, CROI 2025

Urban vs. Rural PrEP users, US 2023

- Used IQVIA Real-World Data
- > 470,000 urban PrEP users received PrEP from >86,000 providers
  - 59% received PrEP from a physician
  - Traveled a median of 6.2 miles to receive PrEP
- >28,000 rural PrEP users received PrEP from >16,000 providers
  - 56.3% received PrEP from NP or PA
  - Traveled a median of 39 miles to urban provider or 36 miles to rural provider
- Distance and providers may be a barrier; consider telehealth and local pharmacies to dispense PrEP to rural users

Zhu et al, Abstract 1223, CROI 2025

Oral PrEP persistence in the US

- Used IQVIA commercial prescription database
- Evaluated PrEP persistence (continuous PrEP for at least 30 days)
- Non-persistence more common in:
  - Women
  - Younger age (compared with 55-64 years)
  - Black, Hispanic, other race/ethnicity
  - Public or cash payment
  - Northeast, South, West (compared with Midwest)
  - 2021-2022 (compared with 2017-2022)
- Only ~40% of new oral PrEP users continued until 6 months
- But, doesn't take into account 2-1-1 users or people switching to CAB-LA

Huang et al, Abstract 1200, 2025

Point-of-care urine tenofovir testing for PrEP adherence

- Young MSM have high HIV incidence and challenges with PrEP adherence are common
- A prior study in Kenyan women of urine point-of-care (POC) tenofovir tests demonstrated improved long-term PrEP adherence
- Study of 49 US MSM <30 years old, randomized 2:1 to POC tenofovir tests with 2 30-minute counseling sessions vs. standard of care; all done virtually
- Of 31 ppts in the intervention arm:
  - 100% successfully self-administered the urine tests
  - 100% reported the intervention was somewhat/very acceptable
- Over 3-month follow-up, increase in hair-levels of tenofovir consistent with 1-2 pill increase per week
  - 6 of 8 intervention participants and 0 of 4 control participants with poor baseline adherence increased to >4 doses/week

Spinelli, Abstract 1212, CROI 2025

CAB-LA uptake in 2 Kaiser systems

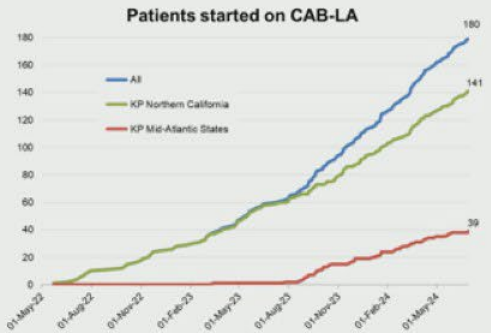
- KP Northern CA and mid-Atlantic states (DC, MD, VA)
  - >5.4 million users
- CAB-LA implemented:
  - Northern CA: May 2022
  - Mid-Atlantic: March 2023
- Compared with oral PrEP users, CAB-LA users:
  - Less likely:
    - Commercial insurance (82% vs. 89%)
  - More likely:
    - Black (19% vs. 10%)
    - Latino (34% vs. 24%)
    - Prior bacterial STI (45% vs. 28%)
    - Hypertension (22% vs. 13%)

Traeger et al, Abstract 191, CROI 2025

Results *Cohort and CAB-LA uptake*

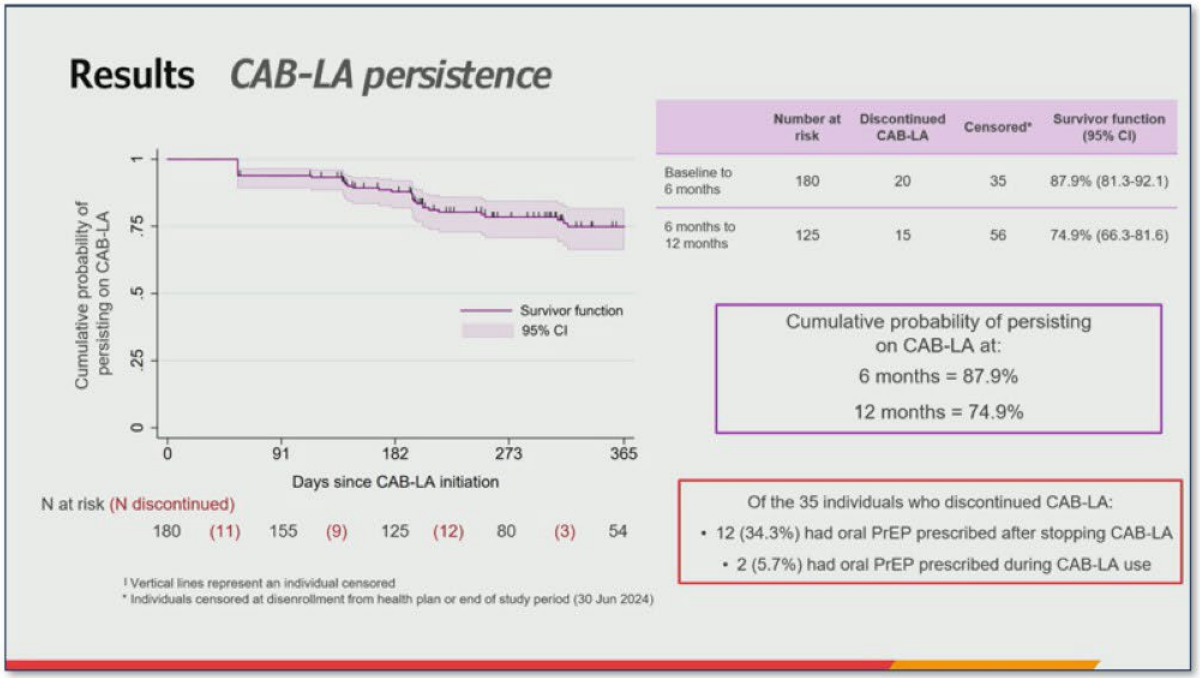
N=23,311
PrEP users
during study period

N=180 (0.8%)
prescribed CAB-LA



Cumulative number of CAB-LA PrEP users
23 May 2022 to 30 June 2024

CAB-LA uptake in 2 Kaiser systems



	Number at risk	Discontinued CAB-LA	Censored*	Survivor function (95% CI)
Baseline to 6 months	180	20	35	87.9% (81.3-92.1)
6 months to 12 months	125	15	56	74.9% (66.3-81.6)

Cumulative probability of persisting on CAB-LA at:

6 months = 87.9%

12 months = 74.9%

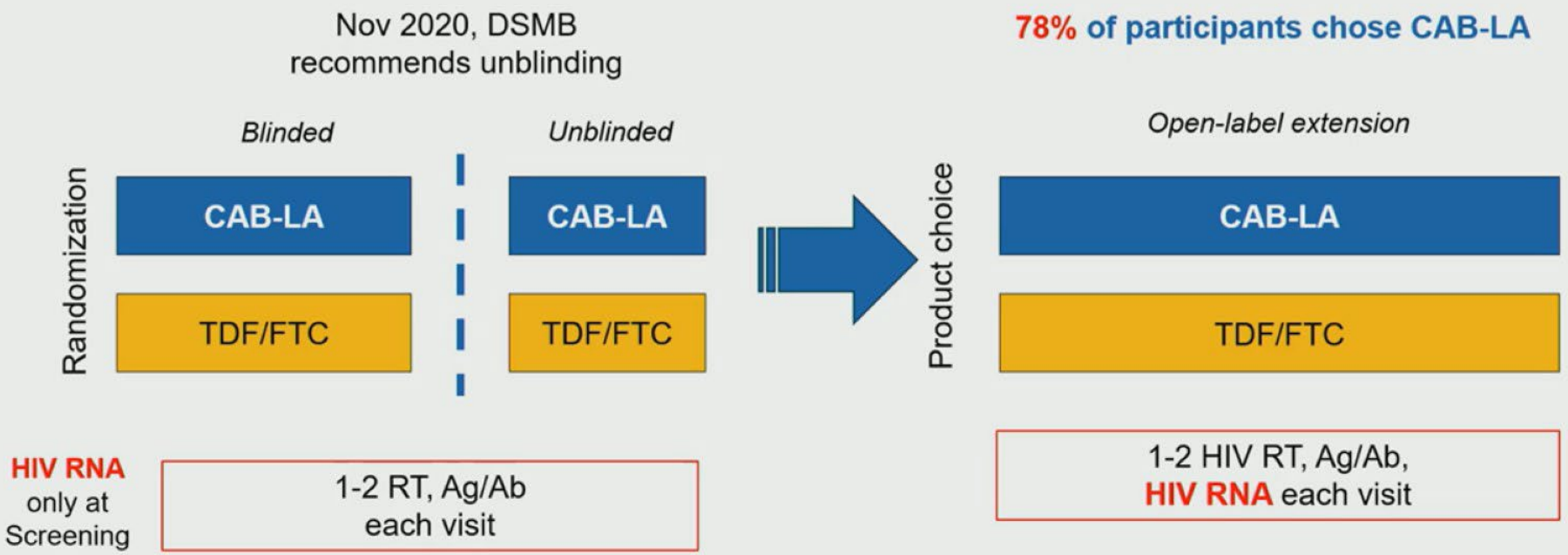
Of the 35 individuals who discontinued CAB-LA:

- 12 (34.3%) had oral PrEP prescribed after stopping CAB-LA
- 2 (5.7%) had oral PrEP prescribed during CAB-LA use

- CAB-LA uptake low, but persistence high
  - >90% on-time or early injections
  - No incident infections
- CAB-LA reaching populations underserved by oral PrEP
  - 24% of CAB-LA users had no history of oral PrEP at Kaiser
- Real-world data guides implementation
  - Late injections more likely after first dose – needs more attention
  - Need to counsel on bridging and switching from CAB-LA to oral PrEP

Traeger et al, Abstract 191, CROI 2025

HPTN 084 study design



Delany-Moretlwe, Abstract 195, CROI 2025

Slide 26

HPTN 084: Results of RNA screening

- Almost 2500 participants included: 1927 on CAB-LA, 535 on TDF/FTC
  - > 24,000 RNA tests (>20,000 on CAB-LA)
- Of these, 87 had ≥1 reactive HIV test
  - 8 (9%) had HIV confirmed
    - 4 of these had isolated RNA+, 3 on CAB-LA, no INSTI resistance
  - 77 (88%) found to be HIV negative
    - 12 of these had isolated RNA+; 5 of whom (42%) had CAB delays > 10 weeks
  - 3 times as many false positives as true positives (12 vs. 4)
  - Unable to differentiate true positive from false positive based on quantification of RNA
- Authors concluded should consider costs & risks in developing testing algorithms

Delany-Moretlwe, Abstract 195, CROI 2025

Breakthrough infections on CAB-LA

- 7 persons diagnosed in clinical care on CAB-LA with breakthrough infection
  - 6 had on-time injections
    - 5 of these had protective levels of CAB
  - 4 had non-reactive HIV Ag/Ab at first detected HIV RNA positive result
  - 5 had INSTI RAMs
    - 1 high-frequency RAMs on population sequencing
    - 4 additional had low-frequency RAMs on sensitive research assay
  - All 7 started on DRV-based ART and have achieved HIV RNA <20 copies/ml
    - 3 with low-frequency RAMs switched to provider selected INSTI-based ART and maintained viral suppression at 13-31 weeks

- Authors concluded long-term follow-up needed to determine the clinical significance of low-frequency INSTI RAMs and durability of viral suppression on INSTI-based ART

Koss et al, Abstract 1228, CROI 2025

Breakthrough infections on CAB-LA

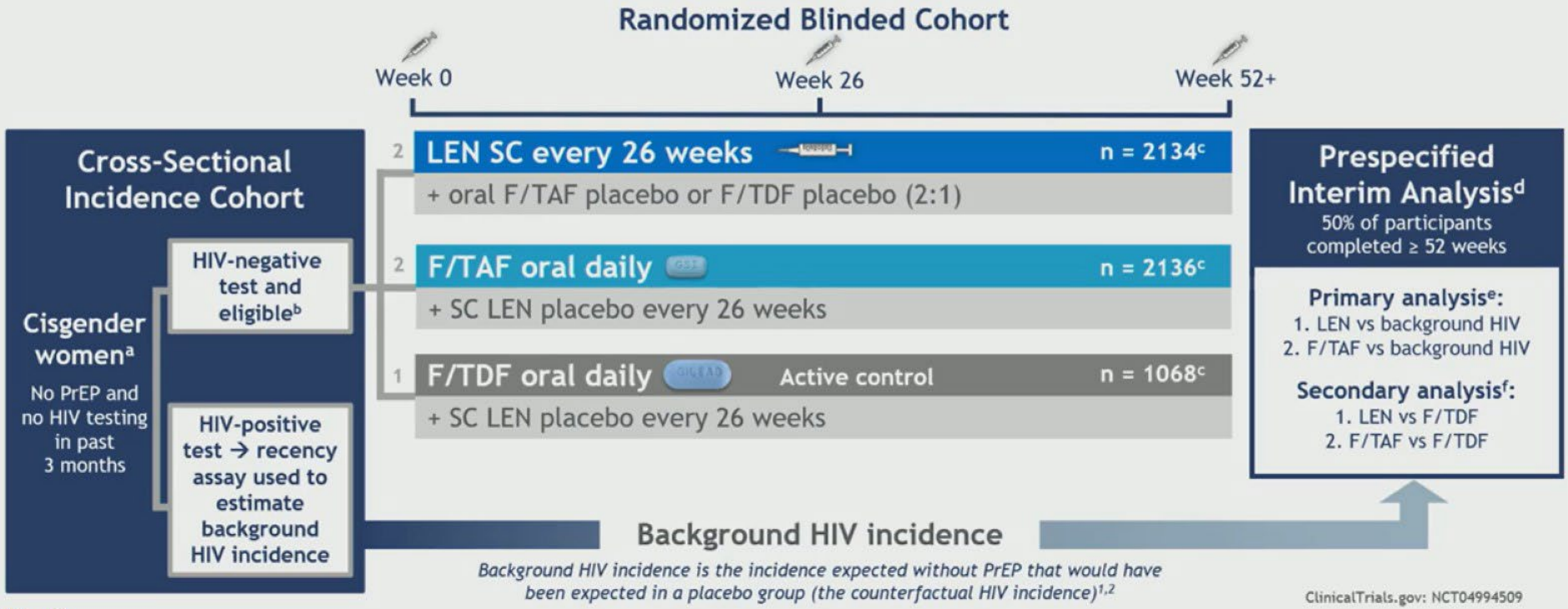
- 47 breakthrough infections in HPTN 083
- Resistance testing and VL done centrally, not available to sites
- Overall, 77% achieved viral suppression (< 50 copies/ml)
  - 71% suppressed on INSTI, 81% on non-INSTI regimens as initial regimen
  - [Additional 3 on INSTI (6%) and 1 on non-INSTI (2%) had VL of 50-78]
  - 5 on non-INSTI regimens switched to INSTI: 4 suppressed, 1 unknown
- 41 ppts had resistance testing available
  - 9 ppts (22%) had INSTI resistance prior to treatment, all suppressed including one with R263K who was started on INSTI
- 2 of 3 without genotyping results failed to suppress, 1 each on INSTI/non-INSTI
- Conclusions: similar results for INSTI vs. non-INSTI regimens but need longer-term f/u

Landovitz et al, Abstract 197, CROI 2025

TAF/FTC in Cisgender Women

Kiweewa et al, Abstract 194, CROI 2025

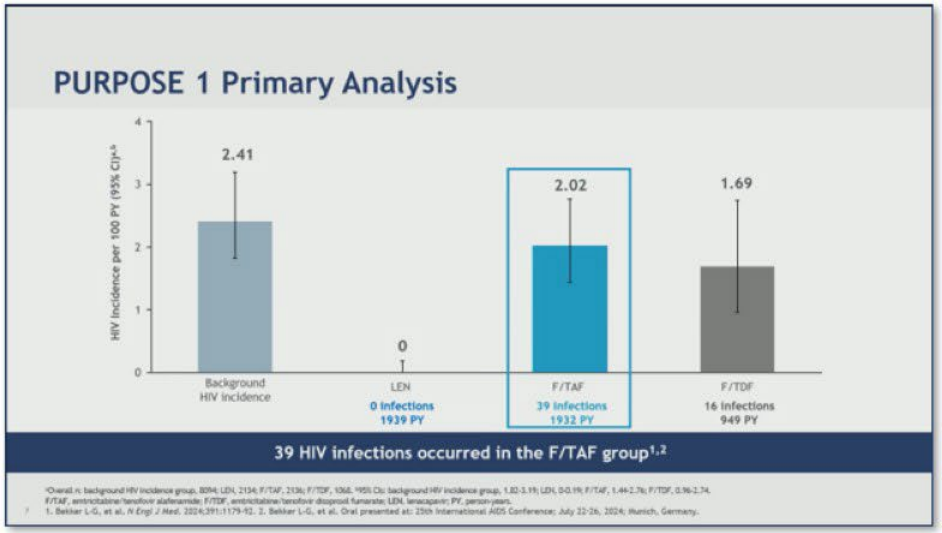
PURPOSE 1 Study Design

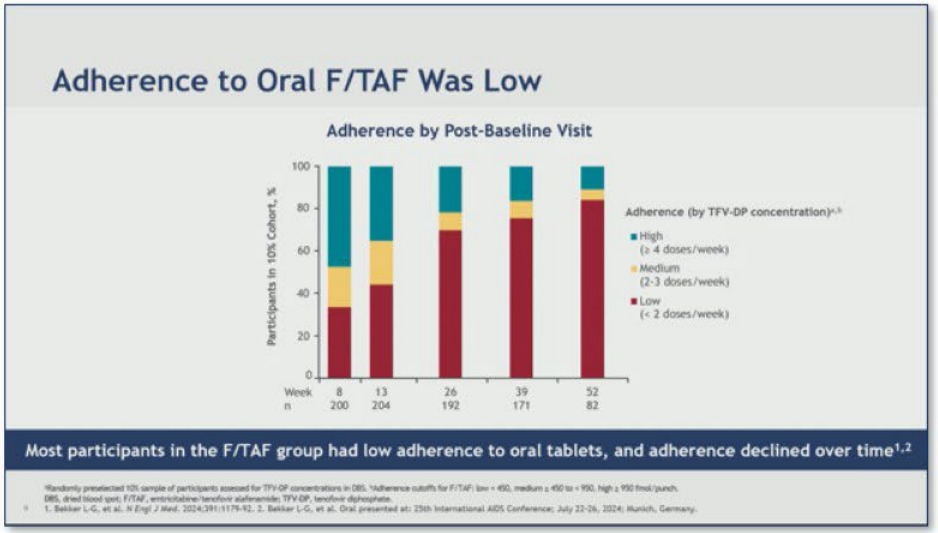


Slide 31

[a]The first participant was screened in August 2021, the 50th-percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. [b]Eligibility criteria included: weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. [d]Since the randomized blinded phase was stopped early due to an efficacy outcome, the interim analysis served as the primary analysis. [e]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[1,2] [f]IRR was assessed using Poisson regression or an exact conditional Poisson regression model in case of zero infections. eGFR, estimated glomerular filtration rate; F/TAF, emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; IRR, incidence rate ratio; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; SC, subcutaneous. 1. Gao F, et al. *Stat Commun Infect Dis.* 2021;13:20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis.* 2024;16:20230004.

TAF/FTC no better than background or TDF/FTC, but poor adherence





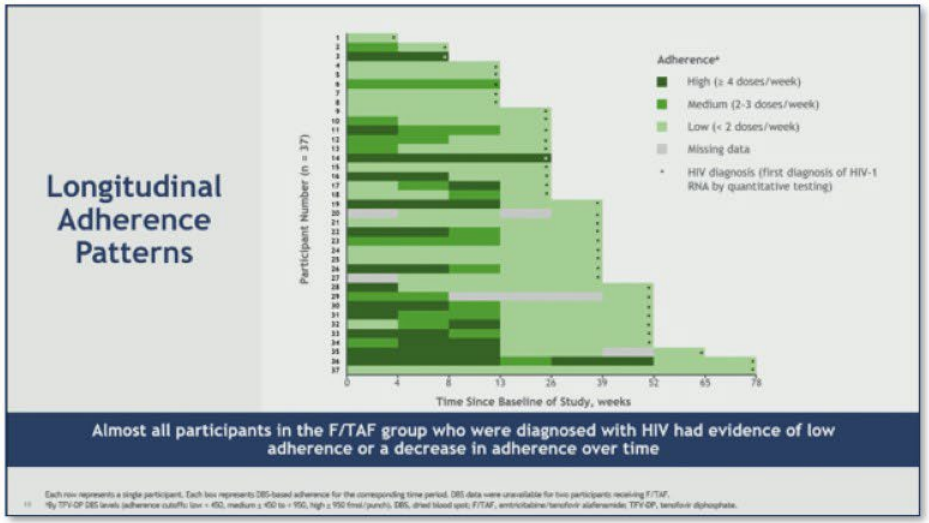
Incidence in F/TAF arm: 2.02
Incidence in F/TDF arm: 1.69
Background incidence: 2.41

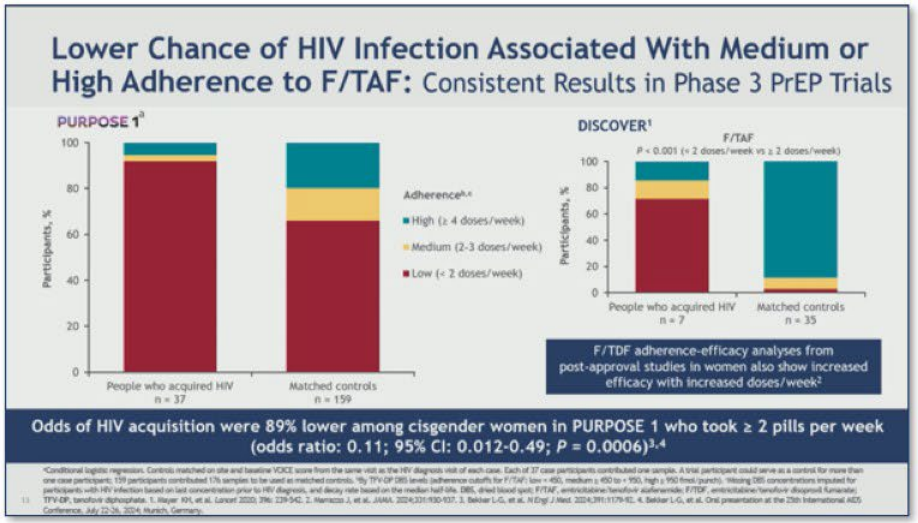
High (≥4 doses/week) and medium (2-3 doses/week) adherence declined over time

Kiweewa et al, Abstract 194, CROI 2025

Slide 32

Poor adherence in those who acquired HIV





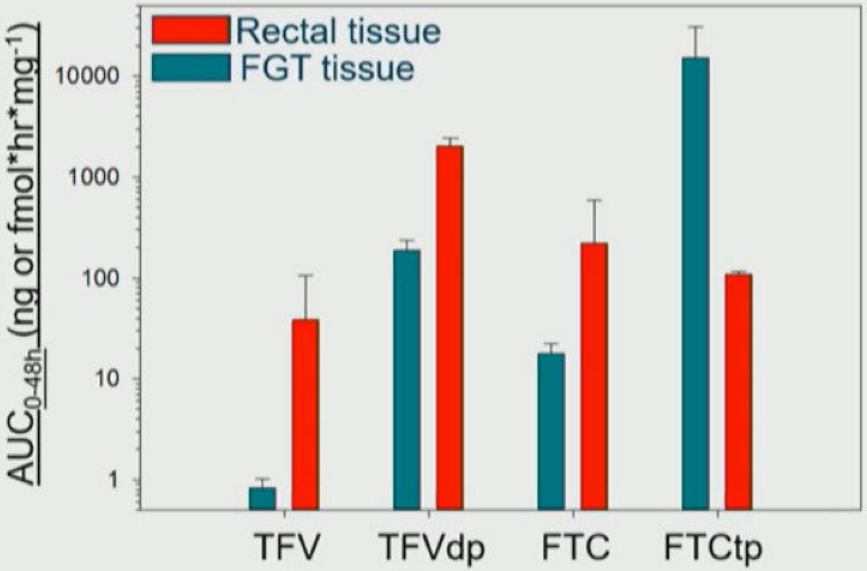
HIV acquisition risk was 89% lower in women who took at least 2 pills/week

Kiweewa et al, Abstract 194, CROI 2025

Slide 33

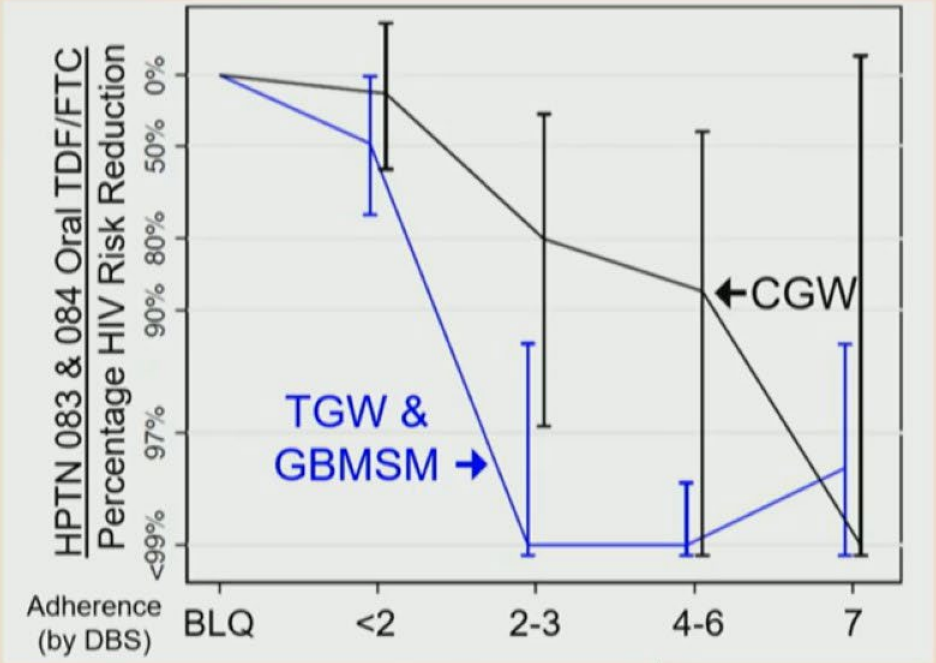
PrEP PK/PD Differs by Site of Action

Tissue **Pharmacokinetics** Differ



Adapted from Cottrell ML et al. *J Infect Dis*. 2016 Jul 1;214(1):55-64.

Tissue **Effectiveness** Differs

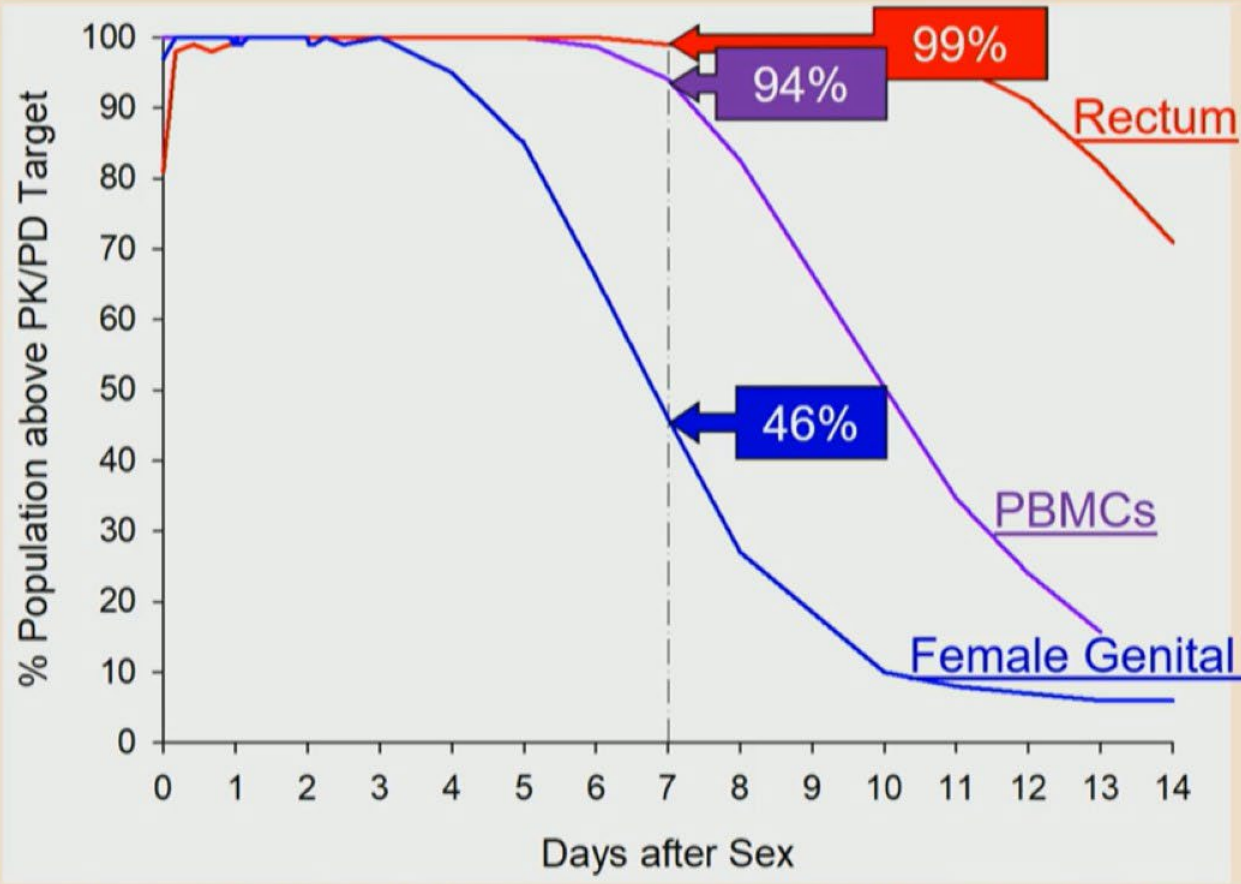


Anderson PL et al. *CID*. 2023 76(10):1850-3.

Cottrell et al, Abstract 157, CROI 2025 Slide 34

CROI 2025

FGT Tissue PK/PD Offers Conservative Prediction



- Predicted that 2-1-1 provides 85% protection for 5 days after sex
- Protection increased (8-15%) if use 2-1-1-1 (add one day)
- Should be explored in clinical trials

Cottrell et al, Abstract 157

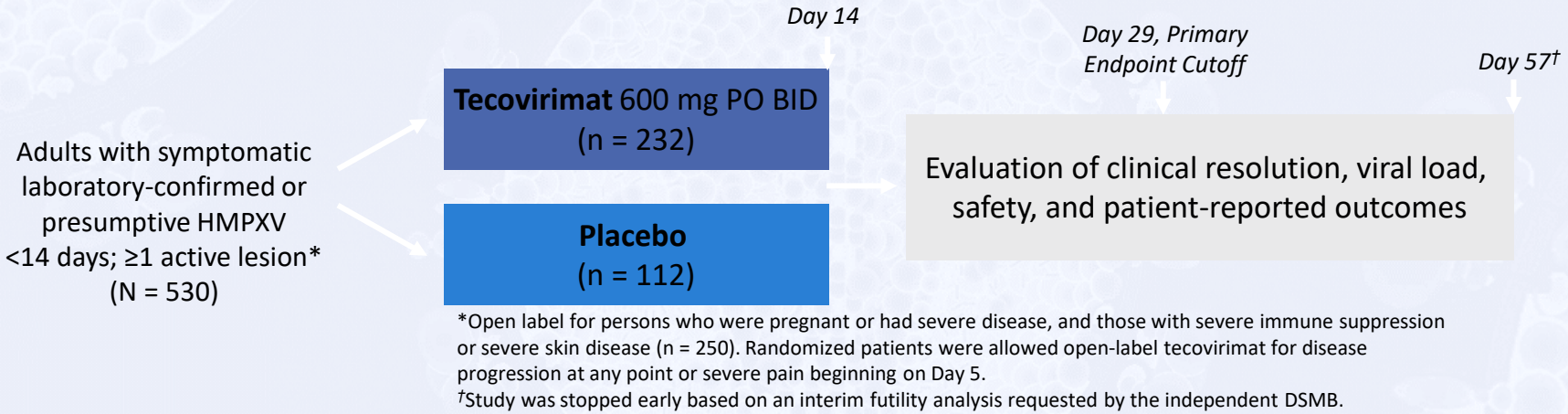
Adapted from Cottrell ML et al. *J Infect Dis*. 2016 Jul 1;214(1):55-64 and Garrett KL et al. J Pharmacol Exp Ther. 2018 Nov; 367 (2):245-251. Slide 35

CROI 2025

STI PREVENTION

STOMP: Study Design

- International, double-blind, placebo-controlled, randomized superiority phase III study



*Open label for persons who were pregnant or had severe disease, and those with severe immune suppression or severe skin disease (n = 250). Randomized patients were allowed open-label tecovirimat for disease progression at any point or severe pain beginning on Day 5.
†Study was stopped early based on an interim futility analysis requested by the independent DSMB.

- **Primary endpoint:** time to clinical resolution (defined as all skin lesions scabbed or epithelialized and all visible mucosal lesions healed) by Day 29
- **Secondary endpoints:** daily pain score, HMPXV detection in various compartments, and patient-reported outcomes (study diary through Day 29, lesion self-assessment, Eq-5d-5L)

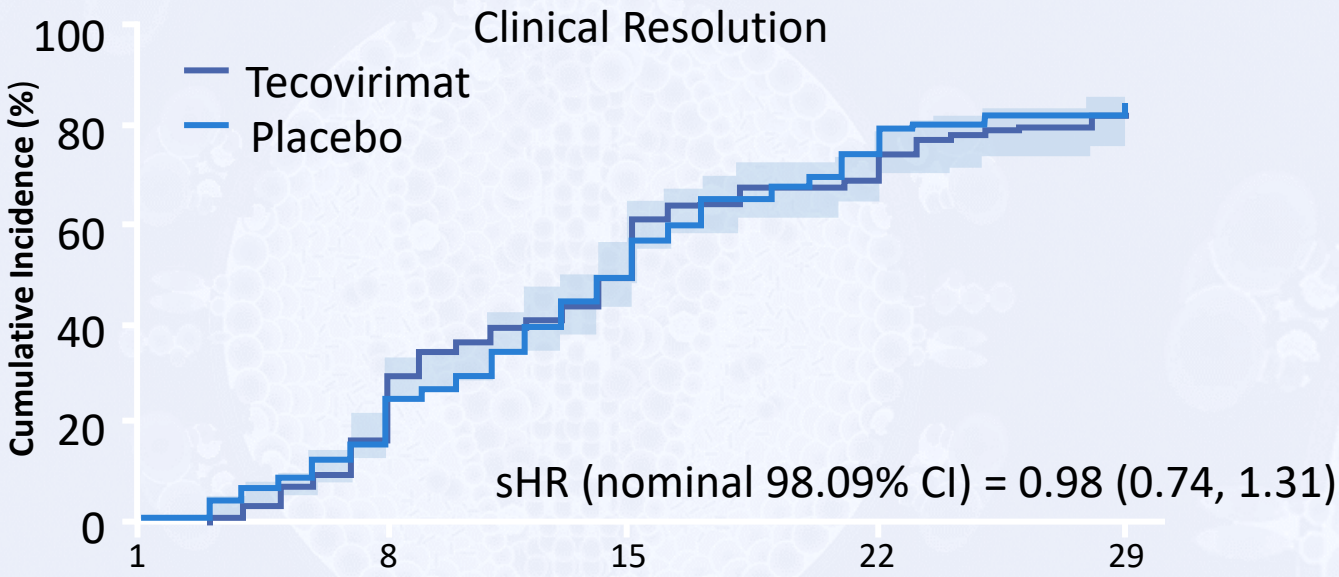
Wilkin. CROI 2025. Abstr 201. NCT05534984.

STOMP: Baseline Characteristics

Characteristic	Tecovirimat (n = 232)	Placebo (n = 112)	Total (n = 344)
Median age, yr (range)	34 (27-40)	34 (28-41)	34 (28-40)
Sex, n (%) ▪ Male ▪ Transgender	 228 (98) 6 (3)	 111 (99) 5 (4)	 339 (99) 11 (3)
Race, n (%) ▪ White ▪ Hispanic	 121 (52) 107 (46)	 61 (54) 44 (39)	 182 (53) 151 (44)
Remote enrollment, n (%)	53 (23)	28 (25)	81 (24)
Time from symptom onset, days (range)	8 (6-10)	8 (6-10)	8 (6-10)
Severe pain (NRS: 7-10), n (%)	81 (35)	35 (32)	116 (34)
Lesions, n (range)	9 (5-18)	8 (3-17)	9 (4-18)
Proctitis, n (%)	85 (37)	37 (33)	122 (35)
Living with HIV, n (%)	86 (38)	31 (28)	117 (35)
Prior smallpox vaccine, n (%)	54 (23)	24 (21)	78 (23)

Wilkin. CROI 2025. Abstr 201.

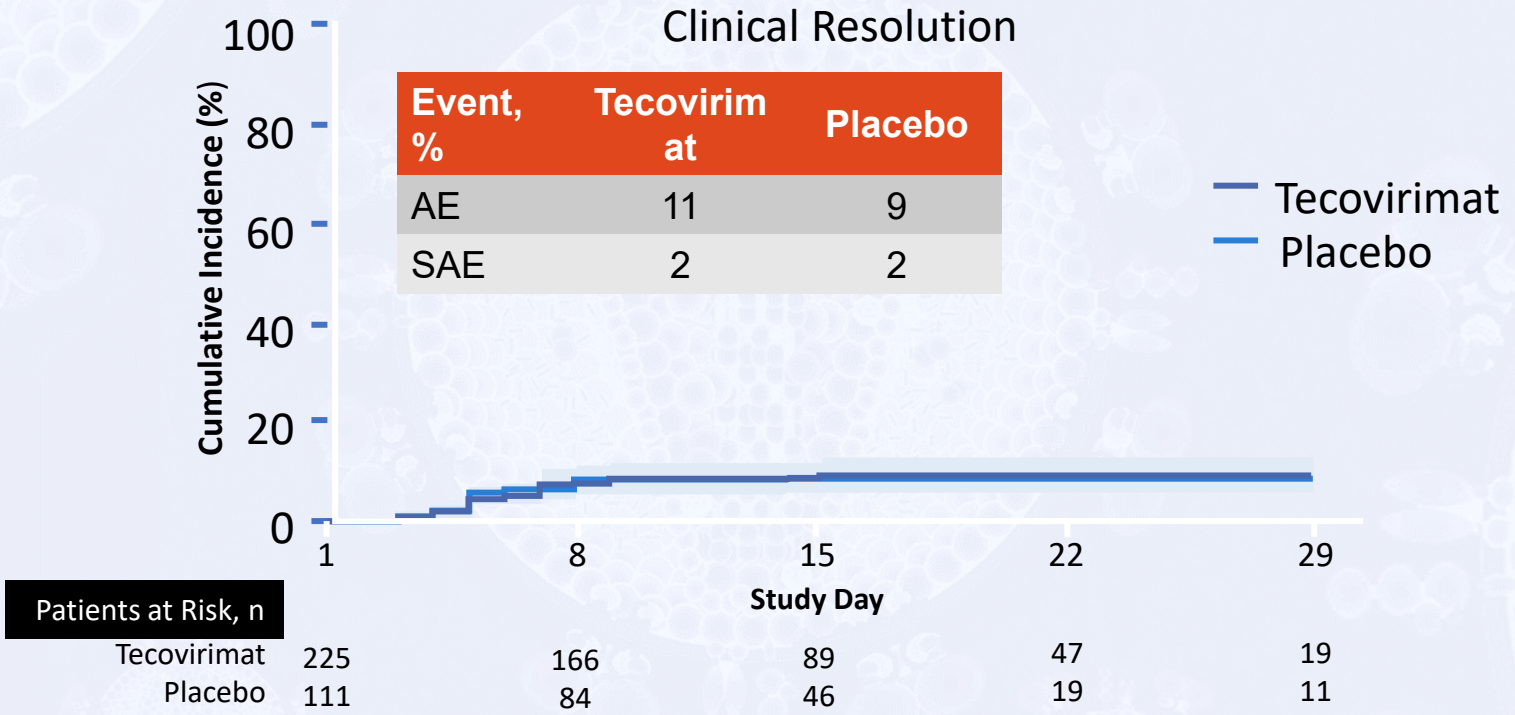
STOMP: Time to Clinical Resolution



Patients at Risk, n					
Tecovirimat	225	166	89	47	19
Placebo	111	84	46	19	11

Wilkin. CROI 2025. Abstr 201. Reproduced with permission.

STOMP: Treatment Switch due to Disease Progression or Severe Pain



Event, %	Tecovirimat	Placebo
AE	11	9
SAE	2	2

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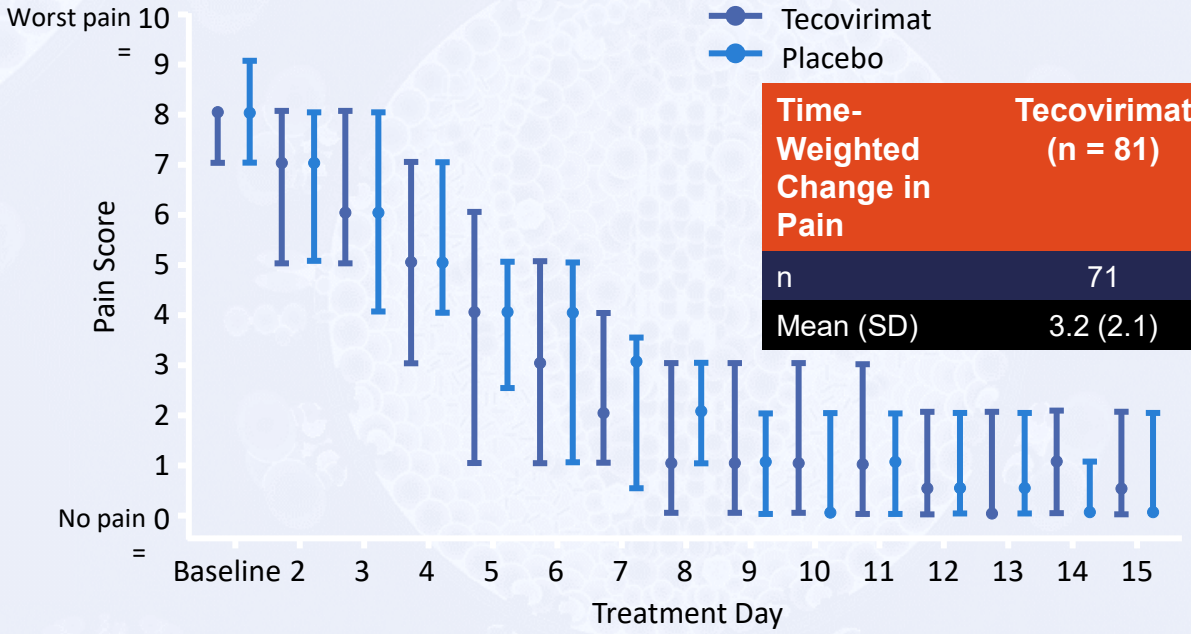
STOMP: Pain Outcomes in Confirmed Mpox and Severe Pain at Baseline



Time-Weighted Change in Pain	Tecovirimat (n = 81)	Placebo (n = 35)	Total (n = 116)
n	71	30	101
Mean (SD)	3.2 (2.1)	3.1 (2.0)	3.2 (2.1)

No. With Measurement	Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Tecovirimat	81	63	66	66	61	58	58	53	54	45	49	46	47	4	4
Placebo	35	29	28	28	28	27	24	23	21	21	20	22	22	8	8
														2	1
														1	9

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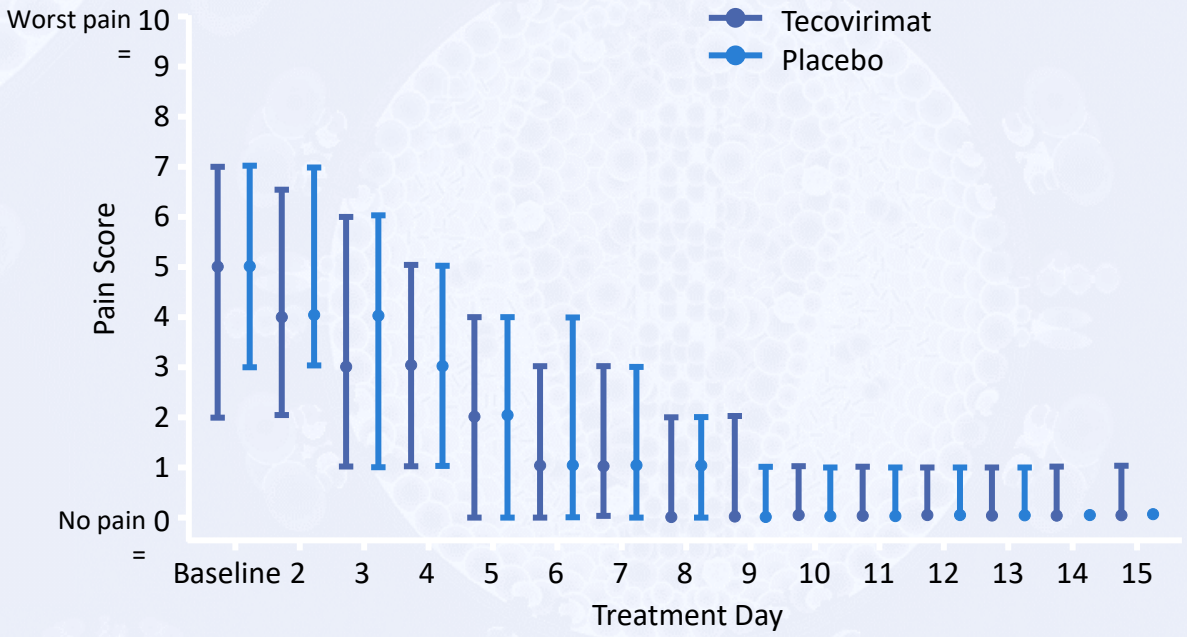
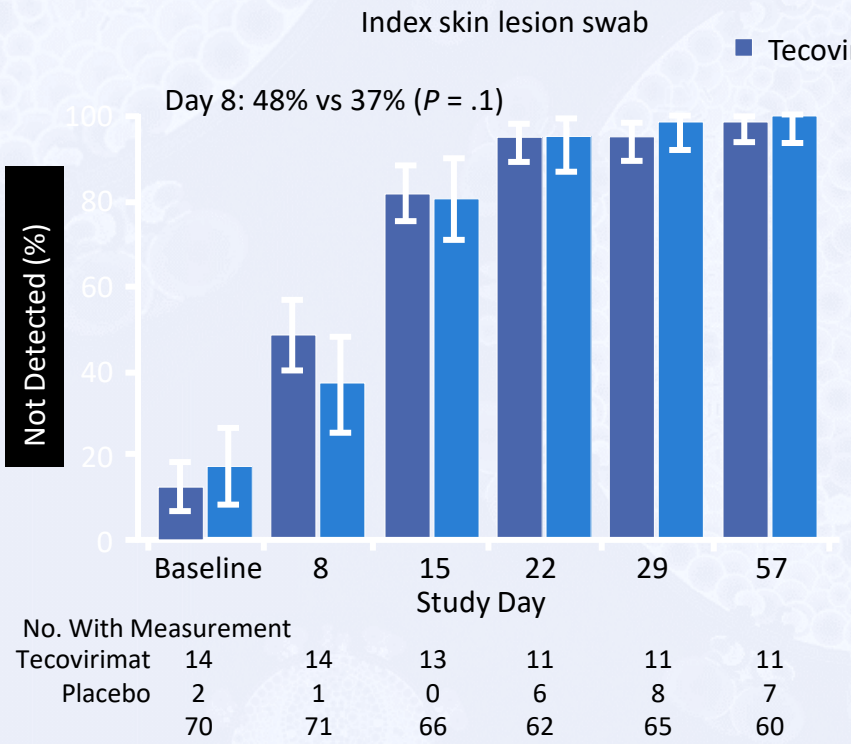
STOMP: Pain Outcomes in Confirmed Mpox



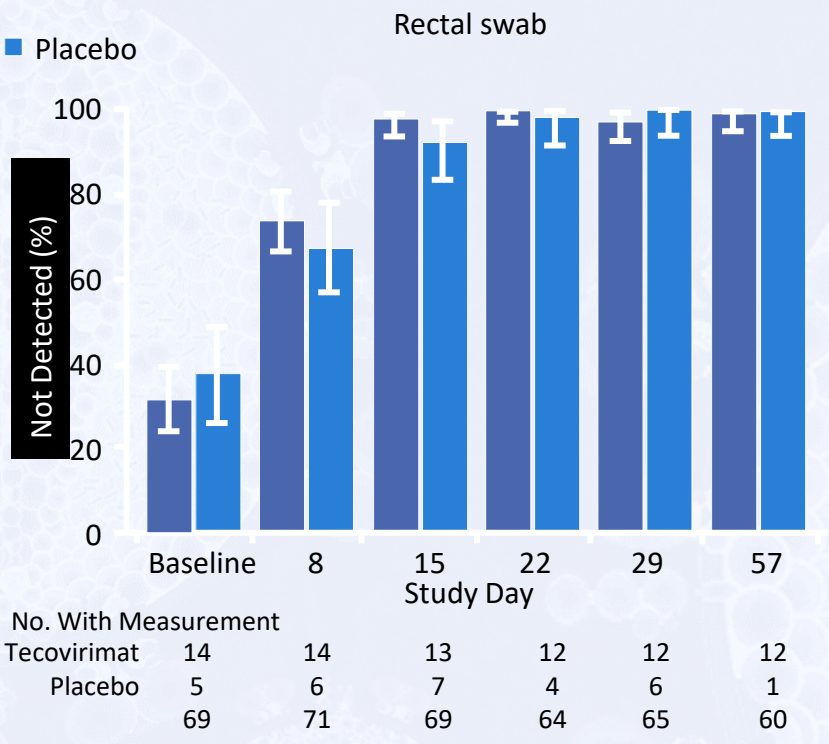
No. With Measurement															
Tecovirimat	232	188	187	185	184	172	172	163	161	152	150	156	152	14	15
Placebo	111	95	92	92	85	84	79	82	76	65	73	71	69	9	1
														69	64

Wilkin. CROI 2025. Abstr 201. Reproduced with permission.

STOMP: Viral Clearance



No. With Measurement						
Tecovirimat	14	14	13	11	11	11
Placebo	2	1	0	6	8	7
	70	71	66	62	65	60



No. With Measurement						
Tecovirimat	14	14	13	12	12	12
Placebo	5	6	7	4	6	1
	69	71	69	64	65	60

Wilkin. CROI 2025. Abstr 201. Reproduced with permission.

Screening for syphilis and HIV in ED

- Screening programs in EDs intended to capture syphilis/HIV in people not seeking regular care
- Hospital instituted screening for all ED pts <65 years; looked 2 years post-implementation; chart review to determine new syphilis and HIV dx
- If tested:
  - Only those who had blood draw for other reasons, miss 17% of new syphilis, 24% of new HIV dx
  - Only those with CBC, miss 24% of syphilis, 33% of HIV dx
  - Only those with GC/CT testing, miss 76% of syphilis, 69% of HIV
- Authors concluded that all targeted screening misses a substantial proportion of new diagnoses, and universal screening should be considered in high prevalence communities

Stanford et al, Abstract 160, CROI 2025

Treatment of syphilis in pregnant women

- Only recommended treatment for late latent syphilis or syphilis of unknown duration during pregnancy is benzathine penicillin G (BPG) in 3 weekly doses
- 7-day intervals between BPG injections is gold standard
- Earlier data suggested 6-8 days doesn't lead to more congenital syphilis (OR 1.0, 95% CI 0.4-3.0)
- CDC STI treatment guidelines imply intervals up to 9 days are acceptable without having to restart full 3-dose series
- California surveillance data (2016-2023) used to analyze 3 groups:
  1. Adequate treatment: BPGx3 at 6-8 day intervals
  2. BPGx3 with at least one 9-day interval
  3. No/inadequate treatment

Johnson et al, Abstract 161, CROI 2025

CS More Likely with 6-9d BPG Intervals vs Adequate Tx

Tx Group	Number of dyads	Number of CS infants	CS incidence proportion	P-value (chi squared test comparing CS incidence)	Odds Ratio (logistic regression)
Adequate tx (6-8d intervals)	677	38 (Suppl Table 3, PMID 37389226)	5.6%	p=0.01 (compared to 9d)	Reference
One or more 9d intervals (no intervals outside 6-9 days)	22	4	18.2%	N/A	3.7 (95%CI 1.2-11.6)
No/inadequate treatment	410	151	36.8%	p=0.08 (compared to 9d)	9.8 (95%CI 6.7-14.4)

Johnson et al, Abstract 161, CROI 2025

Slide 47

Setting

- **San Francisco AIDS Foundation's Magnet Clinic**, a large sexual health clinic in the Castro neighborhood

- >6,000 unique patients seen in 2024
- Diverse clientele – cisgender MSM, transgender and gender diverse
- Of all cases identified in SF City/County in 2021, Magnet diagnosed
  - 15% of early syphilis cases
  - 16% of gonorrhea cases
  - 12% of chlamydia cases

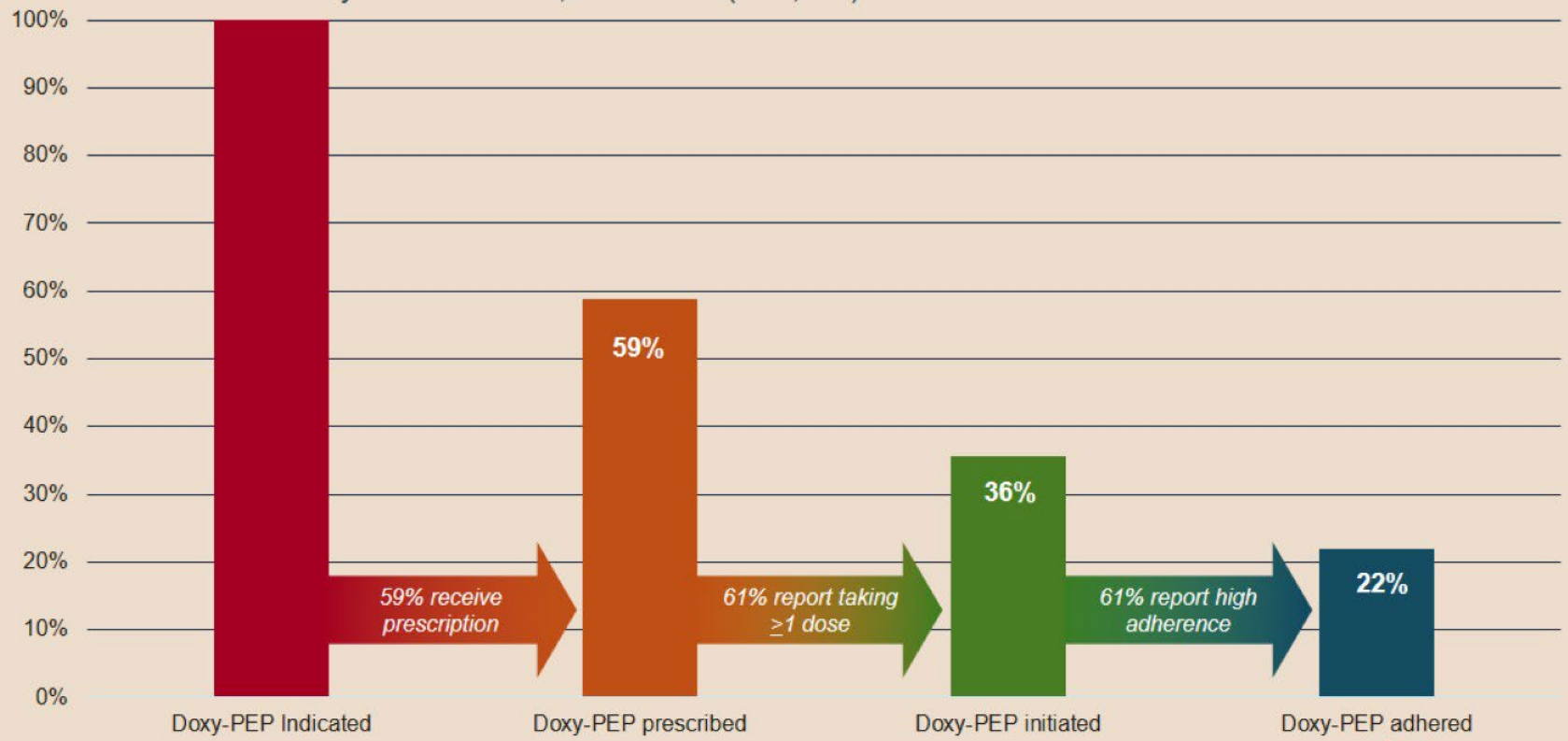
Inclusion Criteria

- Magnet patients with ≥2 visits December 2022-December 2024
- Indication for doxy-PEP using SFDPH guidelines

Barry et al, Abstract 164, CROI 2025

Results – Analysis 1

Figure: Doxy-PEP continuum among patients of the San Francisco AIDS Foundation Magnet Clinic with doxy-PEP indication, 2022-2024 (N=7,436)

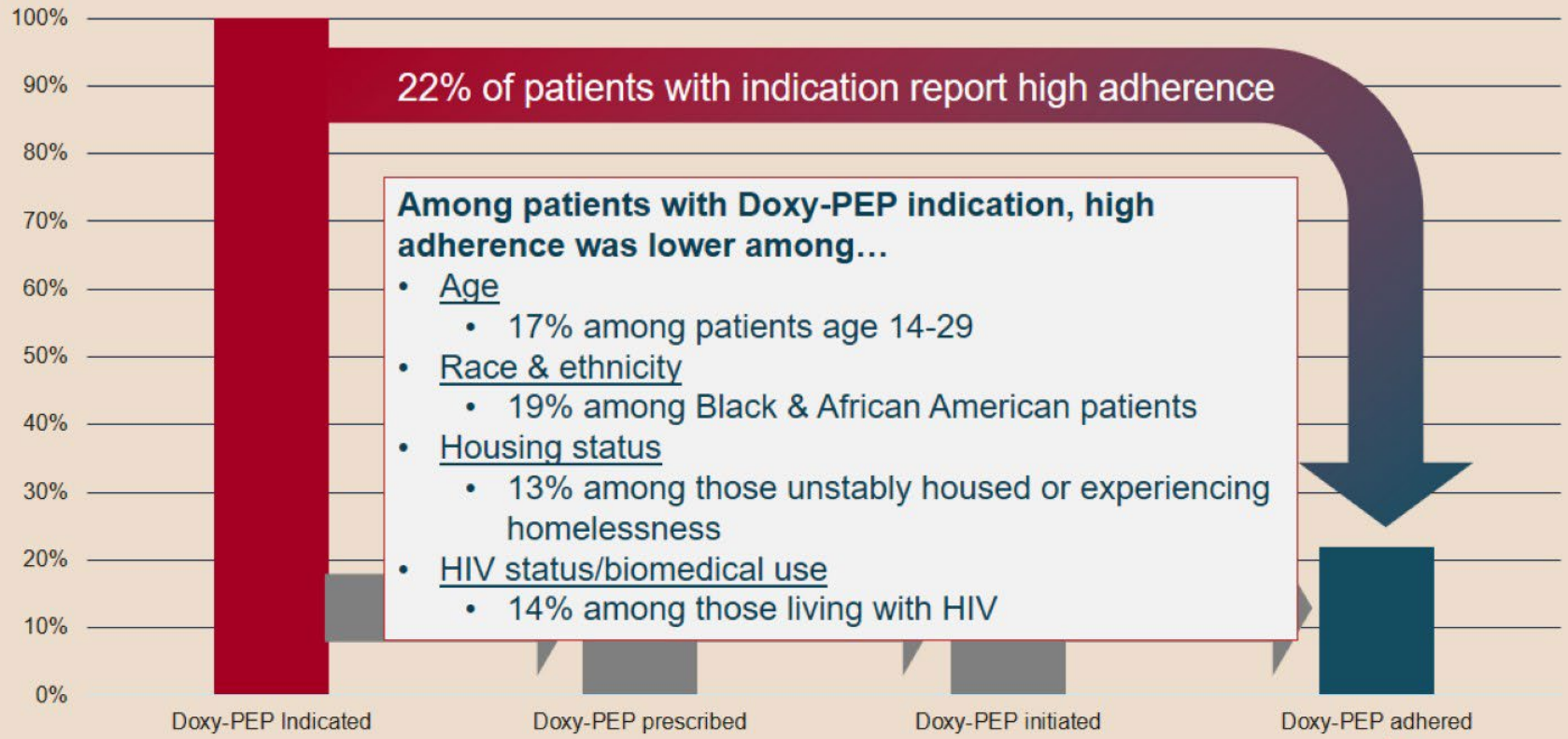


Barry et al, Abstract 164, CROI 2025

Slide 51

CROI 2025

Results – Analysis 2



Barry et al, Abstract 164, CROI 2025

Slide 52

CROI 2025

DoxyPEP for STI Prevention: Study Design

- Observational study of DoxyPEP efficacy on STI incidence over 2 yr at a sexual health clinic in San Francisco
- Enrolled N = 4592 people who used PrEP and had ≥1 visit for sexual health services pre- and post DoxyPEP initiation period
- Compared those who **initiated DoxyPEP** on/after Nov 29, 2022 **(DoxyPEP user)** vs those who **did not initiate DoxyPEP** from Nov 2022 - Sept 2022 **(DoxyPEP nonuser)**
  - **Initiated DoxyPEP:** n = 2524
  - **Did not initiate DoxyPEP:** n = 2068
- STI incidence evaluated each quarter:
  - ≤5 quarters pre- and post-DoxyPEP initiation for users
  - 5 quarters pre- and post-April 1, 2023, for nonusers (median quarter of study period)
- **Main outcomes:**
  - STI incidence pre/post analysis (OR) among **DoxyPEP users** and **nonusers**

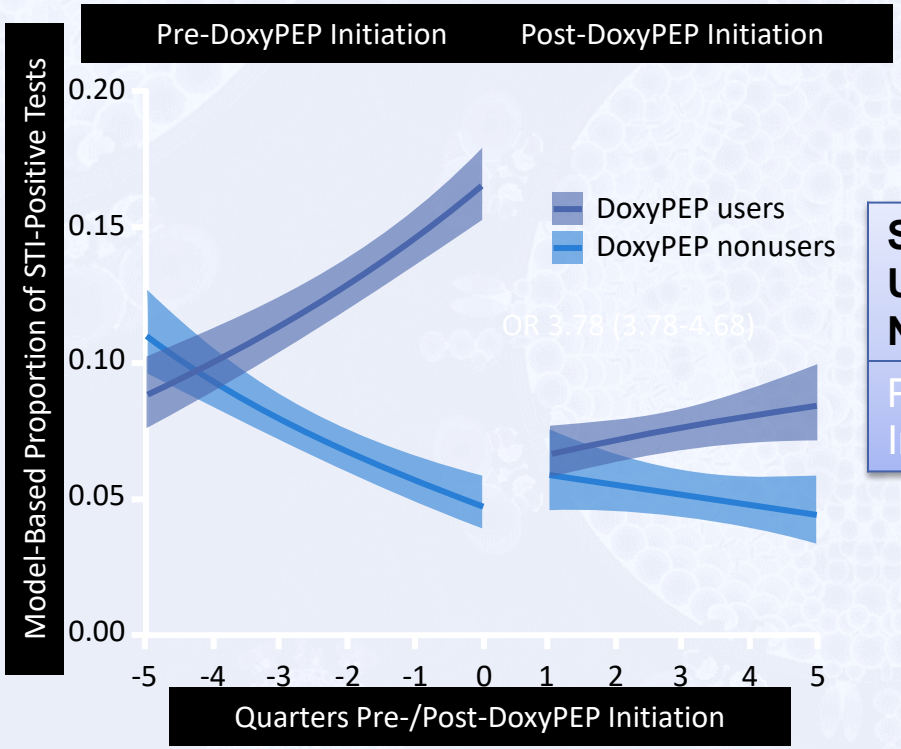
Scott. CROI 2025. Abstr 163.

DoxyPEP for STI Prevention: Baseline Characteristics

Characteristic	DoxyPEP Users (n = 2524)	DoxyPEP Nonusers (n = 2068)	Total (N = 4592)
Median age, yr (SD)	34.9 (10.1)	35.3 (11.1)	35.1 (10.6)
Race/ethnicity, %			
▪ American Indian/Alaska Native	0.3	0.2	0.3
▪ Asian	16.4	16.2	16.4
▪ Black	3.8	5.0	4.3
▪ Hispanic or Latino/a	25.2	22.2	23.9
▪ Multiple	12.4	12.7	12.5
▪ Native Hawaiian/Pacific Islander	0.6	0.7	0.7
▪ White	32.8	34.6	33.6
▪ Declined/other/unknown	5.2	4.9	5.1
Gender, %			
▪ Cisgender women	0.1	1.1	0.5
▪ Cisgender men	90.1	88.6	89.4
▪ Nonbinary	6.0	5.8	5.9
▪ Transgender women	3.0	2.9	2.9
▪ Transgender men	0.7	1.6	1.1
PrEP type, %			
▪ Injectable	2.7	1.4	2.1
▪ On demand	14.6	14.9	14.7
▪ Daily	76.7	77.9	77.2

Scott. CROI 2025. Abstr 163.

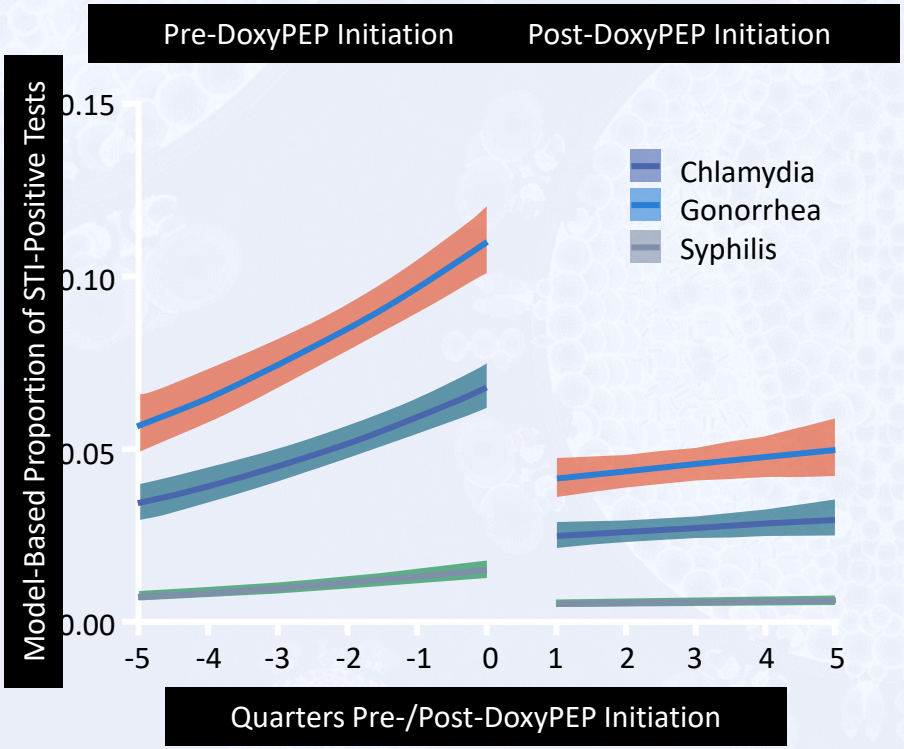
DoxyPEP for STI Prevention: STI Incidence Comparison



STI Incidence in Users vs Nonusers	OR	95% CI	P Value
Pre-DoxyPEP Initiation	3.78	3.04-4.68	<.001

Scott. CROI 2025. Abstr 163. Reproduced with permission.

DoxyPEP for STI Prevention: STI Incidence in DoxyPEP Users



STI Incidence Pre- vs Post-DoxyPEP in DoxyPEP Users	OR	95% CI	P Value
Any STI	0.34	0.28-0.42	<.001
Chlamydia	0.19	0.13-0.29	<.001
Syphilis	0.11	0.02-0.54	.006
Gonorrhea	0.56	0.44-0.71	<.001

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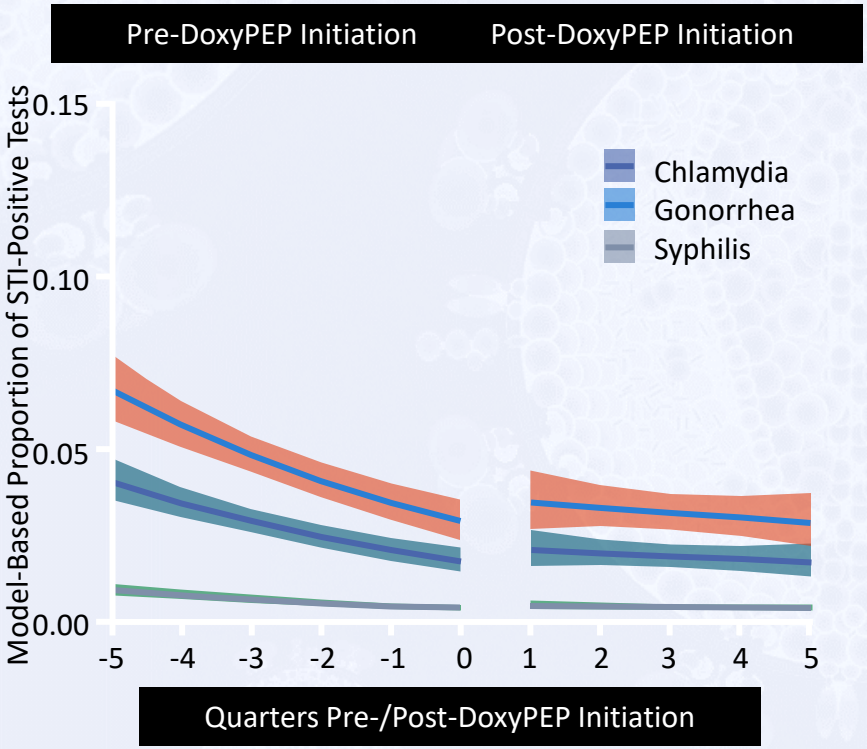
DoxyPEP for STI Prevention: STI Incidence in DoxyPEP Nonusers



STI Incidence Pre- vs Post-DoxyPEP in DoxyPEP Nonusers	OR	95% CI	P Value
Any STI	1.33	0.88-2.00	.178
Chlamydia	1.04	0.54-2.00	.895
Syphilis	1.91	0.11-32.19	.654
Gonorrhea	1.53	0.92-2.55	.099

Scott. CROI 2025. Abstr 163. Reproduced with permission.

The Pipeline…what's coming?

Preferences for LEN vs. daily pill for PrEP

- Women in PURPOSE 1 study of LEN vs. daily TDF/FTC asked about their preference in the future for PrEP modality
- At baseline:
  - 67% preferred twice-yearly injection; ¾ maintained preference through week 52
  - 29% preferred daily pill; ½ maintained preference through week 52
  - 4% no preference
- At week 52:
  - ½ of those who had preference for pills switched to twice-yearly injections
  - ½ of those with no preference switched to twice-yearly injections
- ~60% had greater confidence in their ability to maintain adherence and to feel more protected with twice-yearly injection vs. daily pills (before results of PURPOSE-1 known)
- This demonstrates importance of choice, as preferences change

Mansoor et al, Abstract 1230, CROI 2025

Once-yearly formulation of LEN

Singh et al, Abstract 154, CROI 2025

Study Design

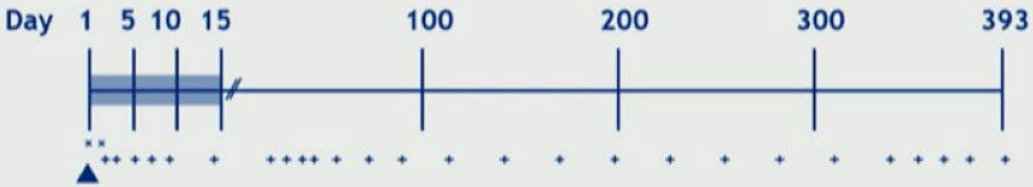
Open-label, Phase 1 study evaluating the PK, safety, and tolerability of a single 5000 mg[a] IM dose of two free-acid LEN formulations: Formulations 1 and 2

Cohort 1: Formulation 1 (5% EtOH; n = 20)

Cohort 2: Formulation 2[b] (10% EtOH; n = 20)

Study Population

- Healthy participants with a low likelihood of HIV acquisition
- Aged 18-55 years
- BMI ≤ 35.0 kg/m²



- Clinic inpatient observation
- ▲ Study drug dosing: two 5-mL IM gluteal injections
- × Intensive PK sample (≤ 5 minutes before dose, and 2, 4, 8,12, 24 and 36 hours post dose)
- \+ Single anytime PK sample[c] follow-up: Days 22-43 (± 1 day), Days 57-141 (± 3 days), Days 169-393 (± 5 days)

Safety Assessments

- Laboratory evaluation
- Investigator-reported AEs
- Participant-reported outcomes including pain measures on a qualitative scale

PK Analysis/Outcomes

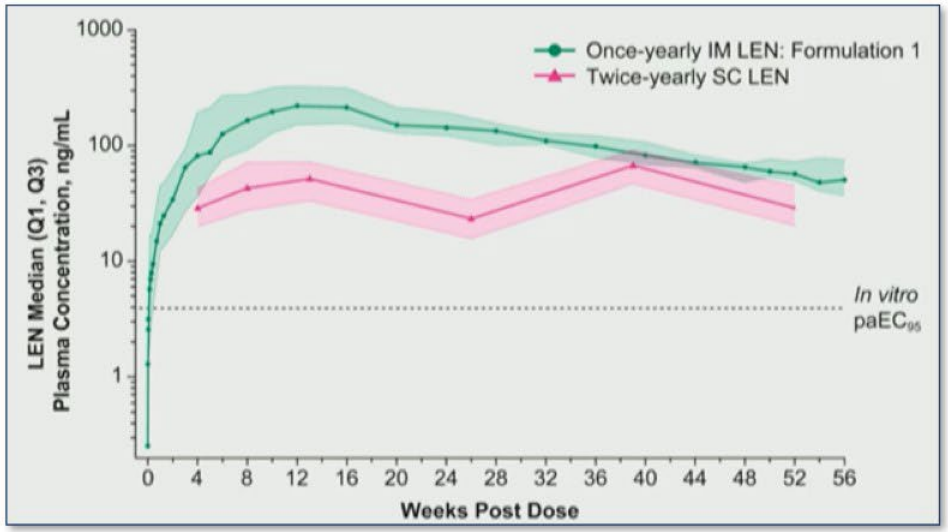
- PK ($AUC_{Days\ 1\text{-}365}$, C_{max}, T_{max}, and C_{trough})
- Compared LEN concentrations between once-yearly IM and twice-yearly SC LEN

[a]2 × 5 mL of 500 mg/mL. [b]Half of participants who received Formulation 2 were pretreated for approximately 10 minutes with an ice pack at the site of injection. [c]A single anytime PK sample was collected on Days 3, 4, 6, 8, 10, 15, 22, 29, 36, 43, 57, 71, 85, 113, 141, 169, 197, 225, 253, 281, 309, 337, 351, 365, 379, and 393, and at the early termination visit (if applicable).

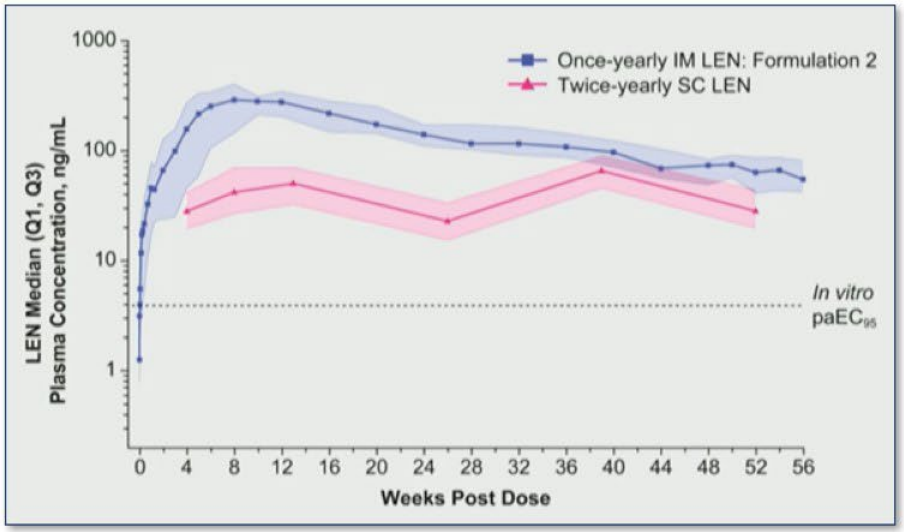
AE, adverse event; **AUC**, area under the concentration-time curve; $AUC_{Days\ 1\text{-}365}$, area under the concentration-time curve for the once-yearly dosing interval calculated from days 1-365; **BMI**, body mass index; C_{max}, observed peak plasma concentration; C_{trough}, estimated trough concentration at the end of 364 days; **EtOH**, ethanol; **IM**, intramuscular; **LEN**, lenacapavir; **PK**, pharmacokinetic; T_{max}, time to reach peak plasma concentration.

Once-yearly LEN formulations maintain higher plasma conc's than twice-yearly LEN thru 56 wks

Formulation 1

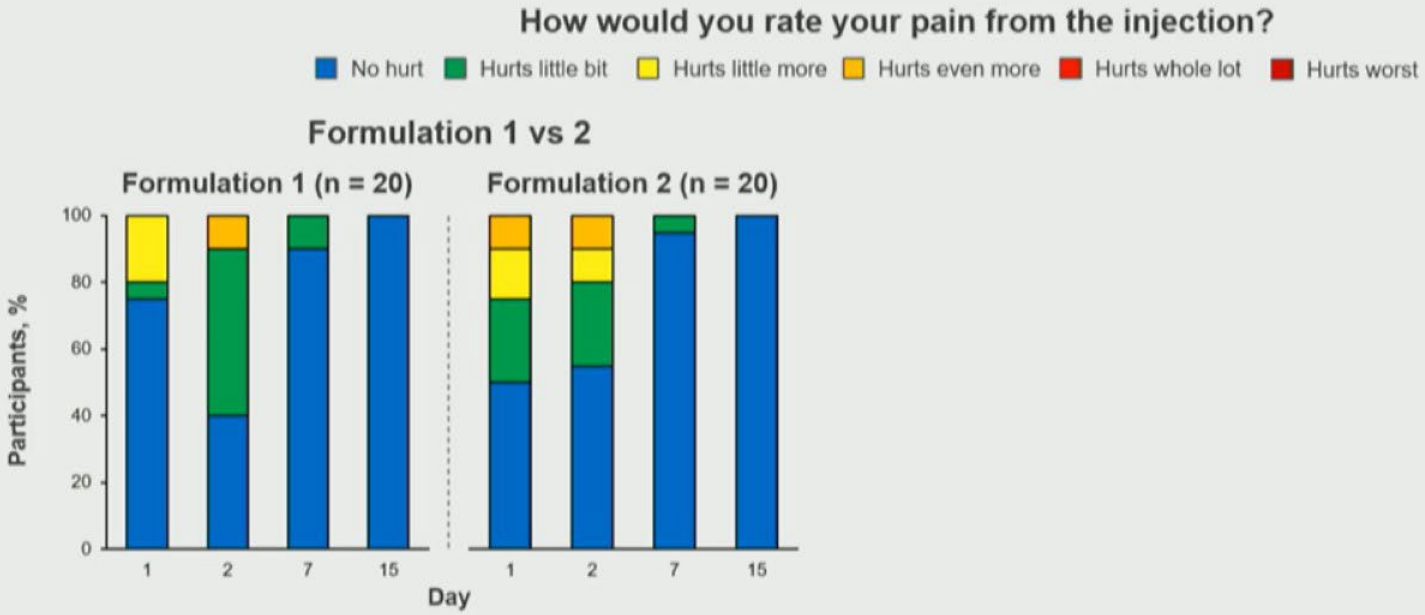


Formulation 2



Singh et al, Abstract 154, CROI 2025

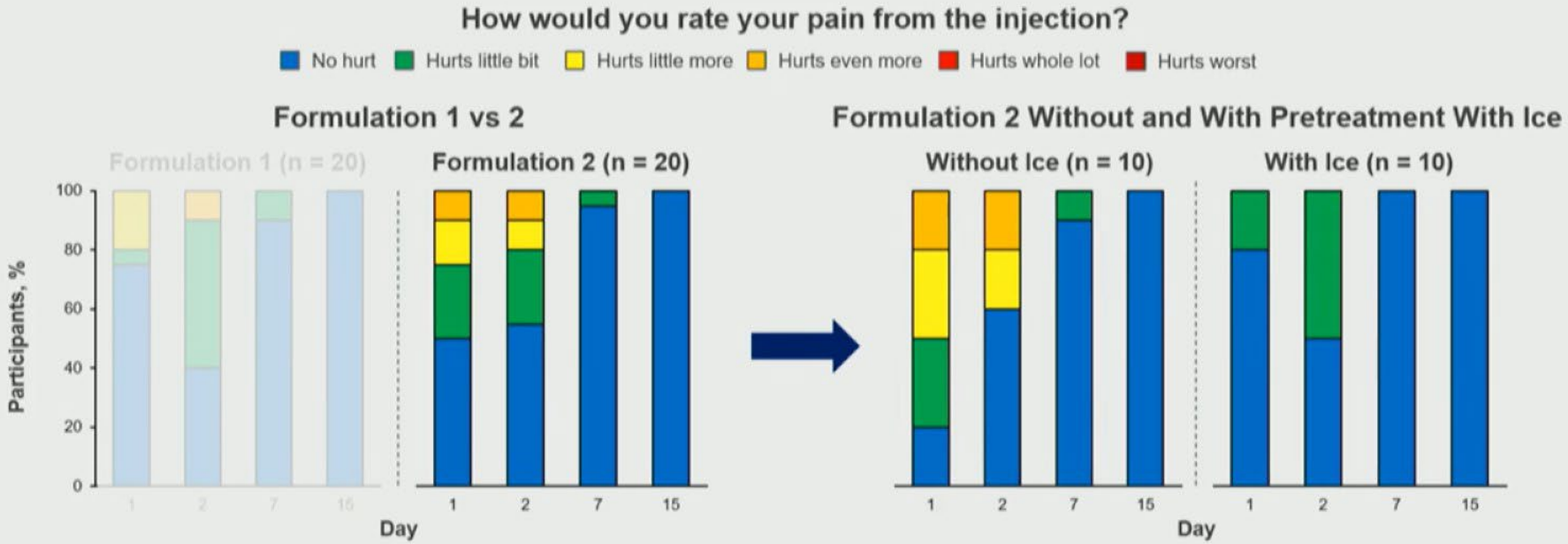
Participant-Reported Injection-Site Pain Diminished Over Time



Most participants reported no or mild pain, which typically resolved within 1 week

Singh et al, Abstract 154, CROI 2025

Participant-Reported Injection-Site Pain Decreased With Ice Pretreatment



Most participants reported no or mild pain, which typically resolved within 1 week
Pretreatment with ice decreased pain ratings on Days 1 and 2 for Formulation 2

Slide 40

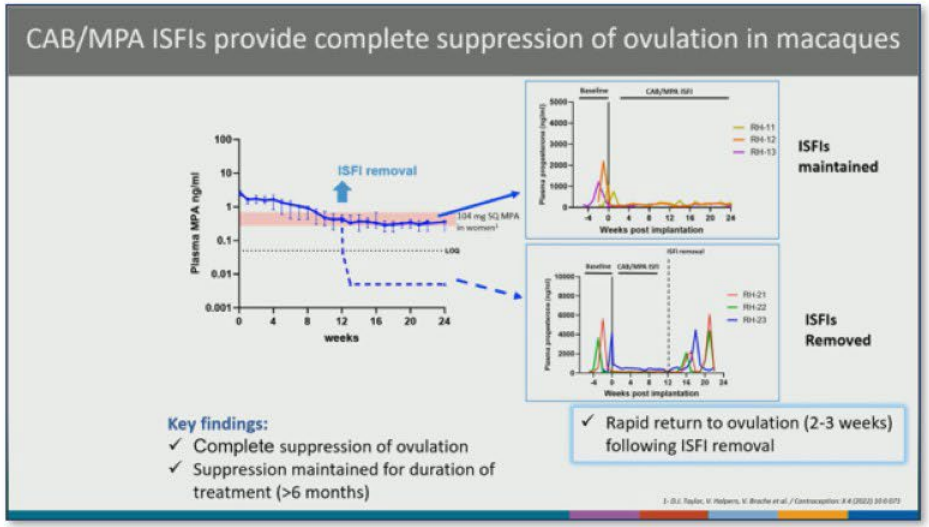
Singh et al, Abstract 154, CROI 2025

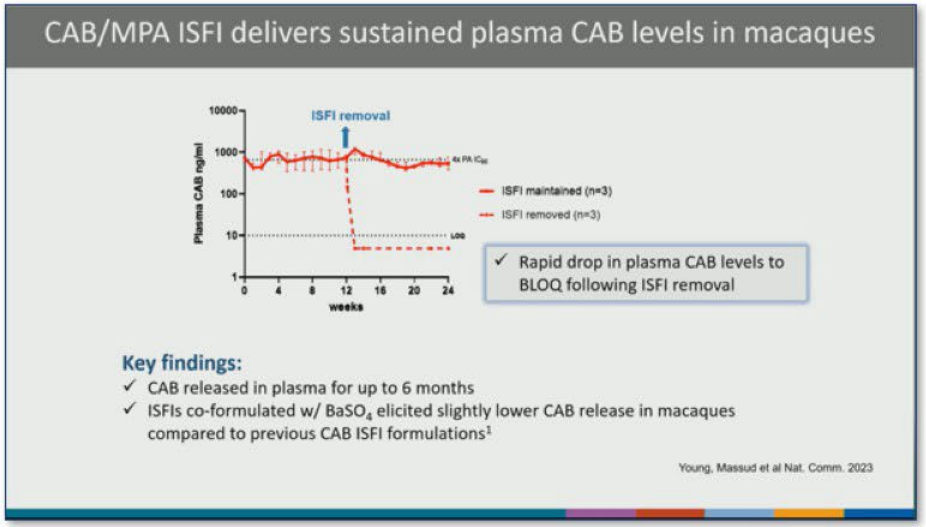
In Situ Forming Implants (ISFIs) as MPT

- Injectable biodegradable copolymer
- Removable with a short PK tail
- ISFIs formulated with CAB provided sustained CAB delivery and long-last protection in NHP
  - In rectal challenge study, 100% protection
  - Sustained delivery of CAB for ~6 months
  - Safe and well-tolerated for >1 year
- ISFI of co-formulated CAB and hormonal contraceptive (MPA)
  - High and sustained concentrations for >180 days
  - Safe and well-tolerated in mice

Massud et al, Abstract 199, CROI 2025; King et al, Abstract 1236, CROI 2025

ISFI suppresses ovulation and delivers CAB up to 6 months



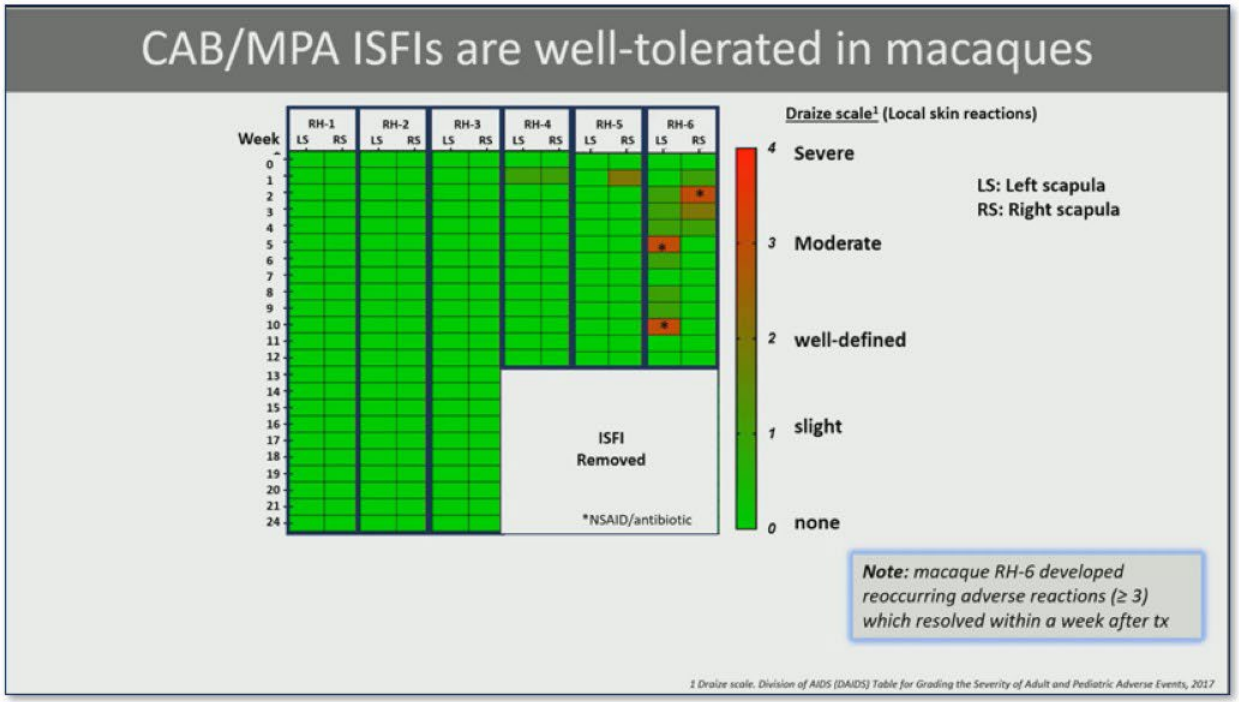


Return to ovulation in 2-3 weeks following ISFI removal

CAB levels drop to BLOQ following ISFI removal

Massud et al, Abstract 199, CROI 2025 Slide 42

ISFIs well-tolerated and do not migrate in macaques



- 1 of 6 macaques had recurrent AEs, resolved within a week after NSAIDs and antibiotics
- X-ray demonstrated:
  - Complete removal @ 3 mos
  - No migration through 6 mos
- Authors state warrants CAB/MPA ISFIs to be tested for women

Massud et al, Abstract 199, CROI 2025 Slide 43

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