Comprehensive Management of Persons Living with HIV in 2023

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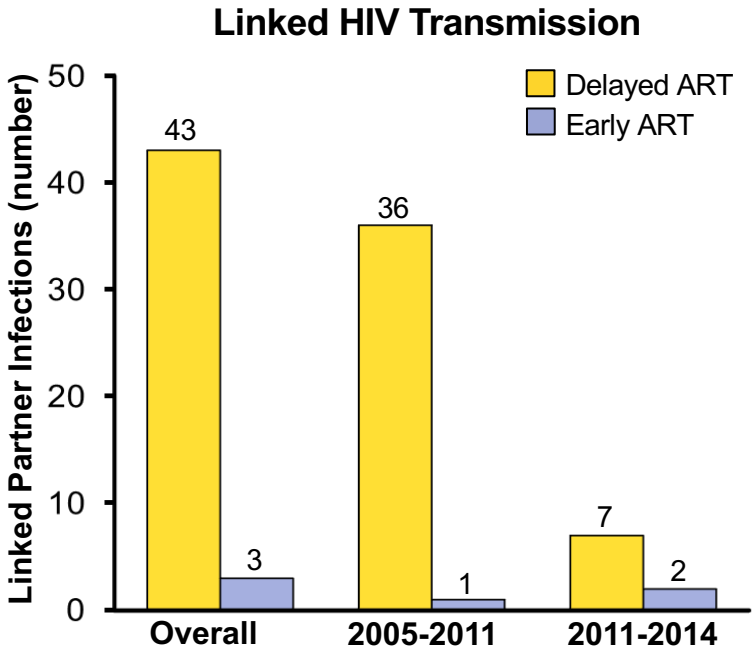
Disclosures: Consultant for Gilead, Merck, ViiV; Research support from Gilead and ViiV; Volunteer member of DHHS Antiretroviral Treatment Panel

Outline

- HIV
  - Prevention
  - Treatment
- STI Prevention
  - DoxyPEP
- HIV Treatment
  - Starting
  - Switching
  - Novel regimens
- Healthy Living with HIV
- Preventing respiratory viral infections

HIV/AIDS and STI Prevention

HPTN 052: Treatment as Prevention



Cohen M ,et al. NEJM 2016; 375:830-839

PARTNER2: HIV Transmission

- PARTNER2: 2014-2018 (MSM only) with 783 discordant couples and 1596 CYFU
- No linked transmissions documented in ~ 77,000 condomless sex acts when HIV-positive MSM partner suppressed to HIV-1 RNA < 200 copies/mL

Sexual Behavior Reported by HIV-Negative Partner	Linked Transmissions, n	Upper 95% CI*	Condomless Sex Acts, n	CYFU
Any sex	0	0.23†	76991	1596
Anal sex	0	0.24	70743	1546
Insertive anal sex	0	0.27	52572	1345
Receptive anal sex without ejaculation	0	0.43	23153	867
Receptive anal sex with ejaculation	0	0.57	20770	652
Any sex with an STI	0	2.74	6301	135

- Unlinked transmissions occurred in 15 initially HIV-negative MSM partners

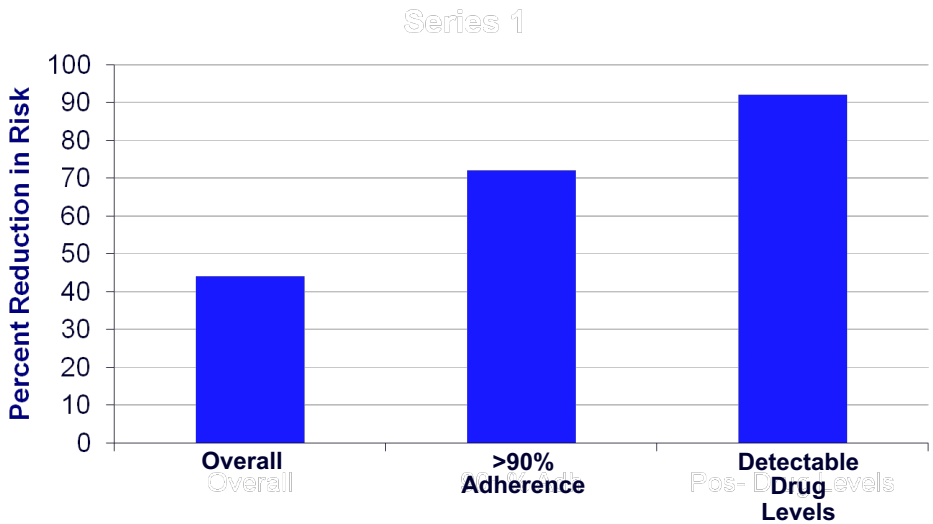
*For rate of within-couple HIV transmission per 100 CYFU. †Compared with 0.84 for MSM and 0.46 for heterosexuals in PARTNER1.

Rodger A, et al. Lancet 2019 3932428-2438.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2010 VOL. 363 NO. 27

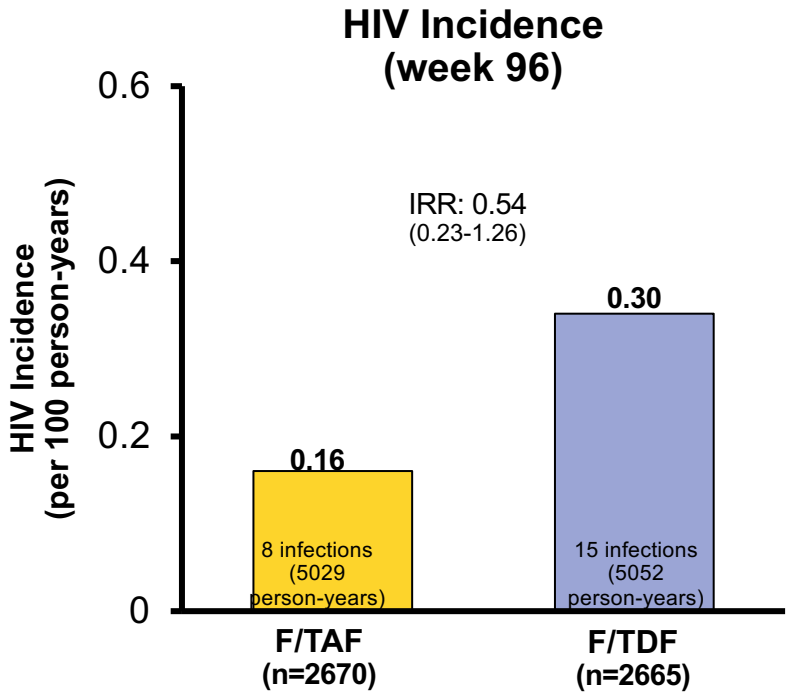
Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men



Grant R. et al. NEJM 2010.

DISCOVER Trial: HIV Incidence at Week 96 With Daily F/TAF or F/TDF for HIV PrEP in MSM/TGW

- F/TAF was non-inferior to F/TDF for HIV prevention at both week 48 and 96
- HIV infections: 23 in 10,081 person-years of follow-up
  - F/TAF (n=8): suspected baseline infection (n=1), low TFV-DP levels (n=6), medium TFV-DP levels (n=1)
    - No FTC or TAF resistance
  - F/TDF (n=15): suspected baseline infection (n=4), low TFV-DP levels (n=10), high TFV-DP levels (n=1)
    - FTC resistance: 4/13 genotyped

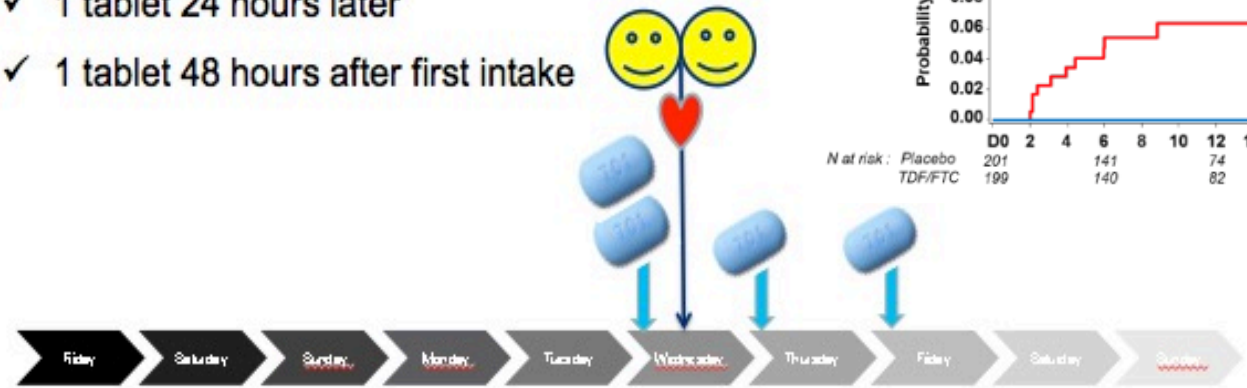


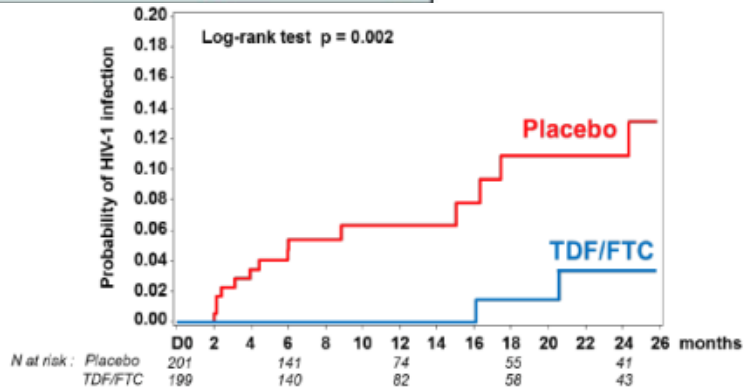
Meyer K, et al. Lancet 2020; 396:239-254

IPERGAY : Sex-Driven iPrEP

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

- ✓ 2 tablets 2-24 hours before sex
- ✓ 1 tablet 24 hours later
- ✓ 1 tablet 48 hours after first intake





4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse

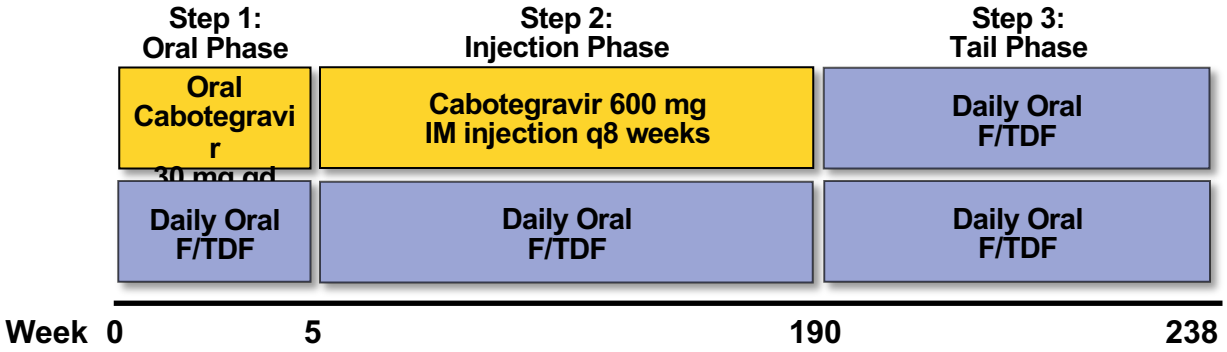
Molina JM, et al. NEJM 2016

LA PrEP: HPTN 083 and HPTN 084

Phase 3 studies

Double-blind, double-dummy, active controlled
Persons at high-risk for HIV infection
In general good health
No IDU, HCV, HBV, seizure disorder, CVD, abnormal liver function

HPTN 083: MSM/transgender women
HPTN 084: cisgender women

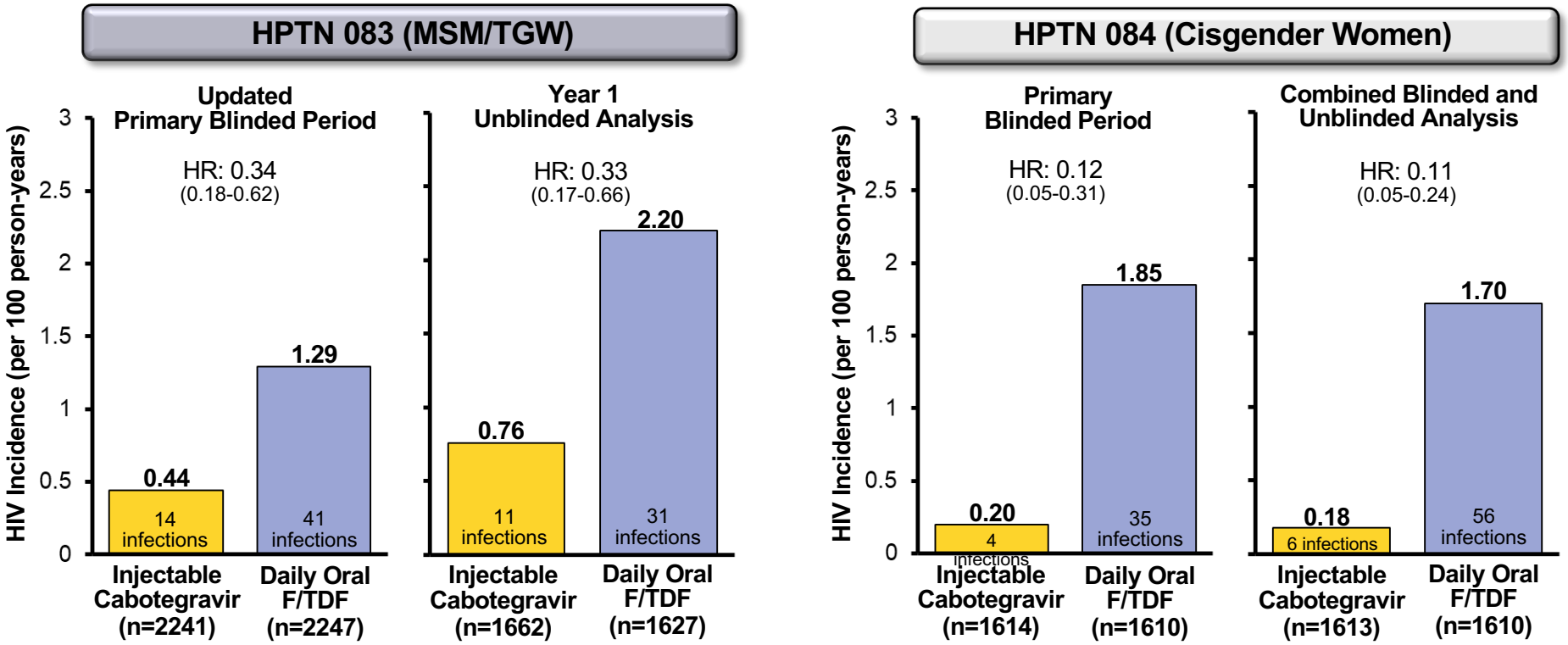


DSMB recommended early termination of blinded phase of both studies

Matching oral and IM placebos included in the oral and injection phase double-blind arms.
HPTN 083 was conducted in US, Brazil, Peru, Argentina, South Africa, Vietnam, and Thailand.
HPTN 084 was conducted in Botswana, Kenya, Malawi, South Africa, Swaziland, Uganda, and Zimbabwe.

Landovitz RJ, et al. *N Engl J Med*. 2021;385:595-608.
Delany-Moretlwe S, et al. *Lancet.* 2022;399:1779-1789.
Delany-Moretlwe S, et al. *J Int AIDS Soc.* 2022;25(suppl 3):227-228. Abstract OALBX0107.

HPTN 083 and HPTN 084 Infection Rate

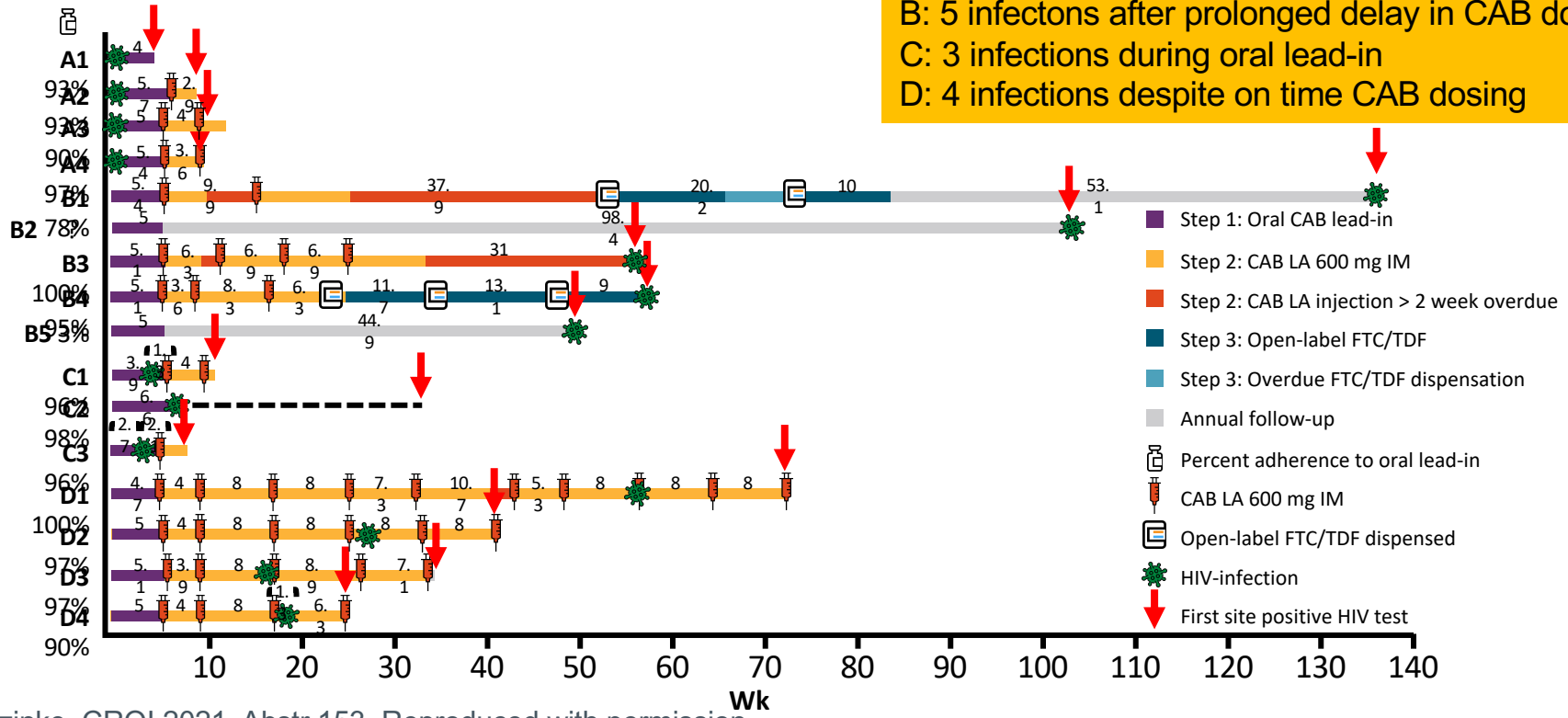


Landovitz RJ, et al. *N Engl J Med*. 2021;385:595-608.
Delany-Moretlwe S, et al. *Lancet.* 2022;399:1779-1789.
Delany-Moretlwe S, et al. *J Int AIDS Soc.* 2022;25(suppl 3):227-228. Abstract OALBX0107.

HPTN 083: LA CAB vs. TDF/FTC

- 4 baseline and 12 incident HIV infections observed in CAB arm

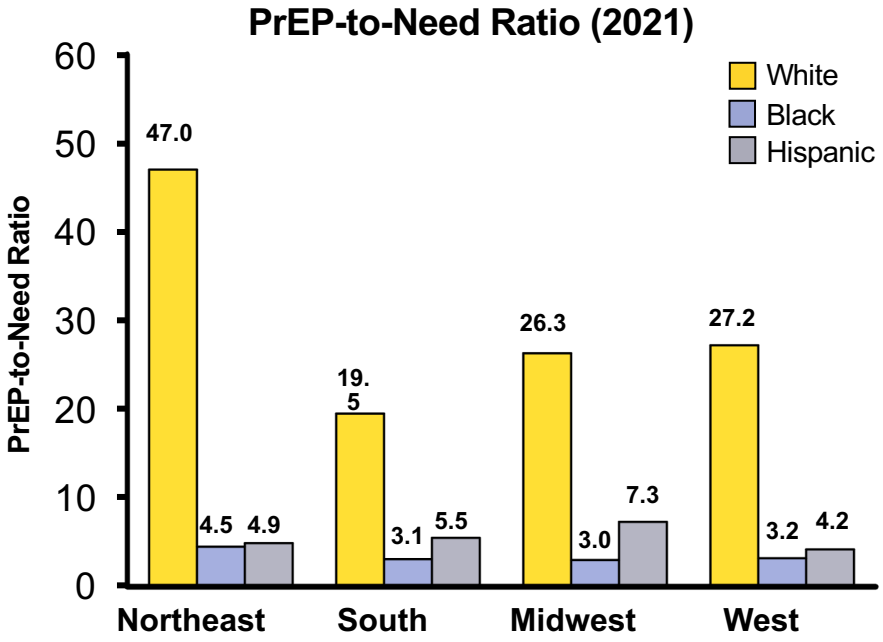
A: 4 baseline infections
B: 5 infectons after prolonged delay in CAB dosing
C: 3 infections during oral lead-in
D: 4 infections despite on time CAB dosing



Marzinke. CROI 2021. Abstr 153. Reproduced with permission.

Trends in PrEP Use in the United States (2012-2021)

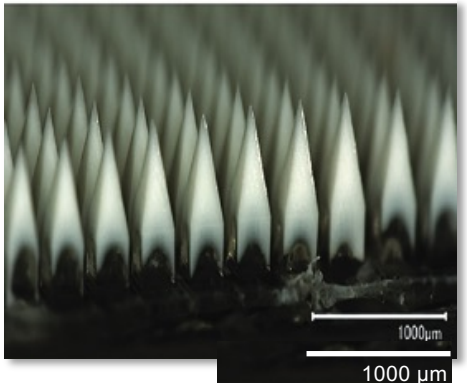
- PrEP-to-need ratio
  - Number of PrEP users divided by the number of new HIV diagnoses in that group in the same year
  - Equity metric, no “target” level
- US prevention programs in all regions have demonstrated larger gaps in PrEP-to-need ratios by race/ethnicity
  - Southern states lagged all other regions
- Better programs are needed to provide PrEP to communities and people at greatest risk for HIV infection



Sullivan P, et al. AIDS 2022. Abstract OALBX0104.

Future LA PrEP options

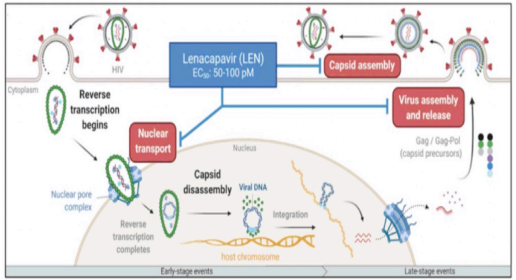
Microarray patch



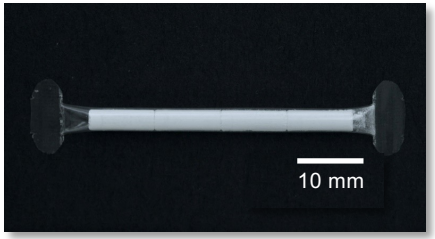
Cabotegravir LA (reformulation)

- Double-strength concentration (400 mg/mL)
- Phase 1 study of safety/ tolerability
  - Subcutaneous (abdominal)
  - Intramuscular (gluteus medius and vastus lateralis)

Lenacapavir (q6 months)



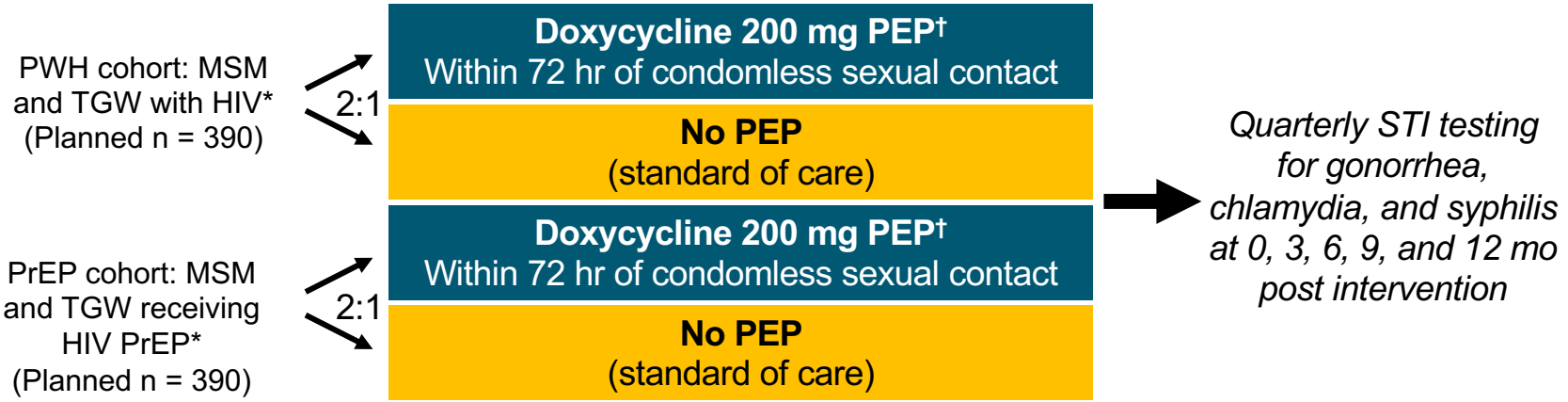
Cabotegravir Implant (non-biodegradable, retrievable)



Rein-Weston A, et al. *Open Forum Infect Dis*. 2019;6(suppl 2):S996. Abstract LB 8.
Benn P, et al. *J Int AIDS Soc.* 2022;25(suppl 3):125-126. Abstract PESUB24.
Hope TJ, et al. *J Int AIDS Soc.* 2021;24(suppl 1):12-13. Abstract OA04.04.

DoxyPEP: Study Design

- Randomized, open-label study conducted at HIV and STI clinics in San Francisco and Seattle

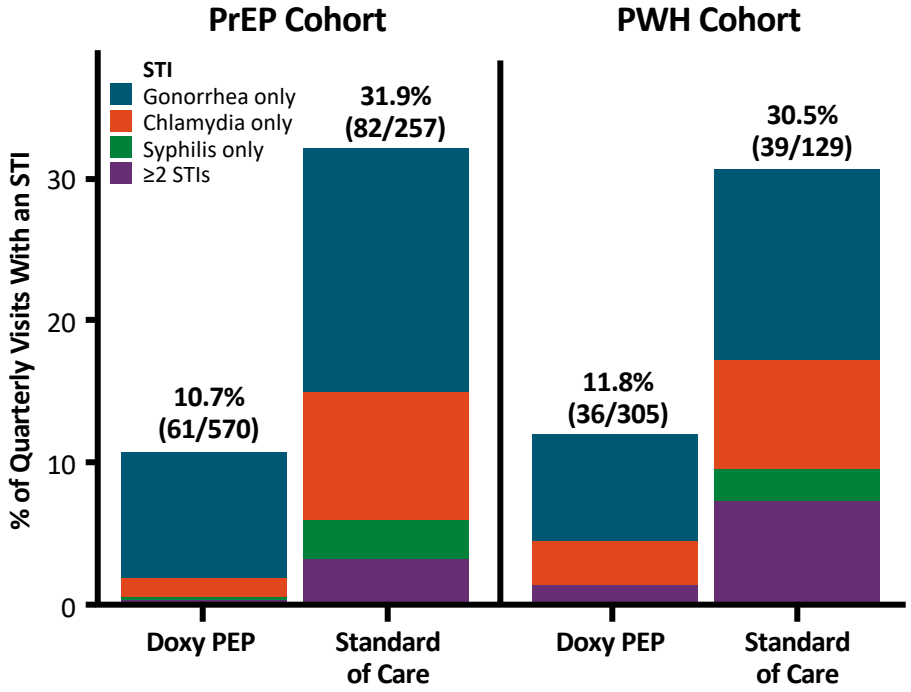


*All participants were assigned male sex at birth, had ≥1 STI in past 12 mo, and had condomless sex with ≥1 partner in past 12 mo.
†Maximum dose of 200 mg/24 hr.

- **Primary endpoint:** ≥1 incident STI (gonorrhea, chlamydia, or syphilis) during quarterly STI test
- **5/13/2022:** Enrollment stopped early per DSMB after interim analysis showed significant effectiveness in both cohorts

Luetkemeyer A, et al. NEJM 2023; 388: 1296-1306

DoxyPEP: Quarterly STI Incidence (Primary Endpoint)



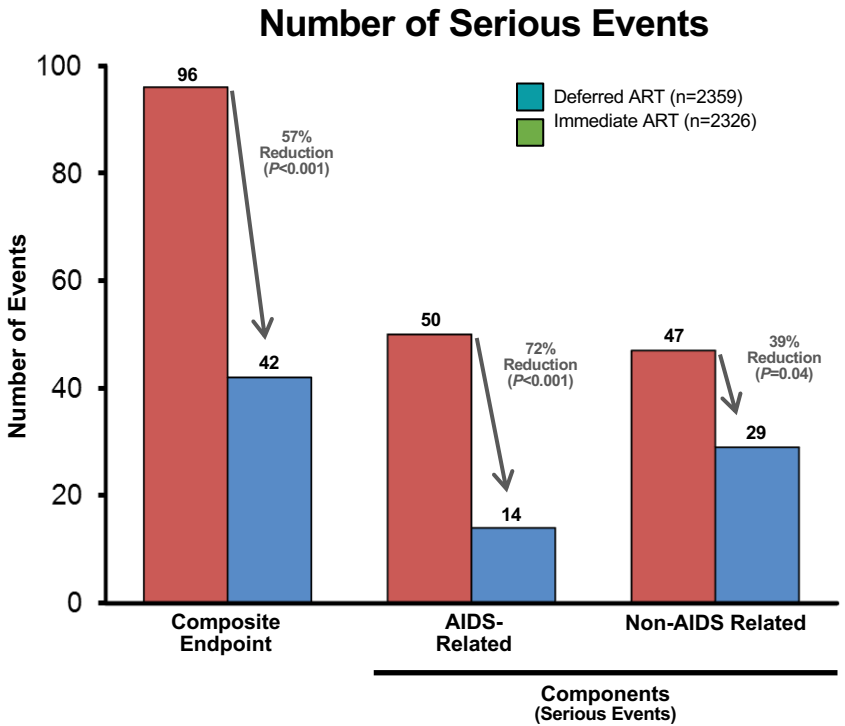
Risk Reduction in STI Incidence per Quarter (95% CI)	Doxy PEP vs Standard of Care*
PrEP	0.34 (0.24-0.46)
PWH	0.38 (0.24-0.60)
Total	0.35 (0.27-0.46)

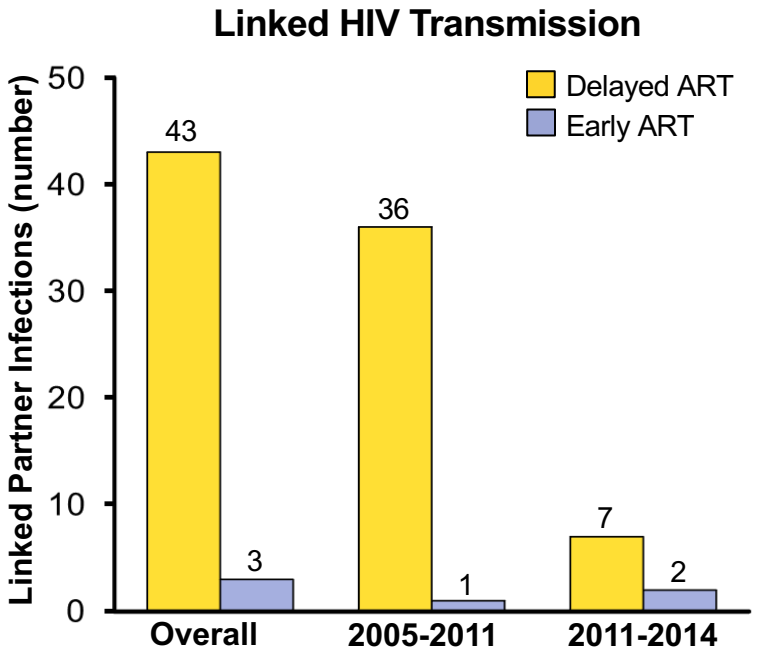
*All P <.0001

Luetkemeyer A, et al. NEJM 2023; 388: 1296-1306

HIV/AIDS Treatment

When to Start: START and HPTN 052 Studies





Lundgren JD, et al. NEJM 2015; 373:795-807; Cohen M ,et al. NEJM 2016; 375:830-839

What Do the Guidelines Recommend for Rapid ART?

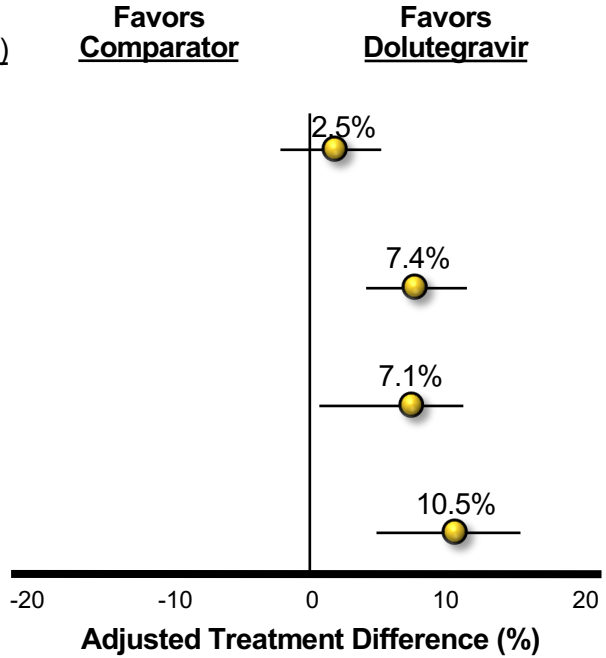
- **DHHS:** ART should be started immediately or as soon as possible following diagnosis[1]
  - Should not include an NNRTI, ABC, or DTG/3TC
- **IAS-USA:** Recommended for all ambulatory patients committed to starting ART as soon as possible after diagnosis[2]
  - Caveats in setting of possible opportunistic infection
  - Should not include an NNRTI or ABC

Rapid ART, or starting ART immediately or as soon as possible following diagnosis, can be started without labs or resistance testing

1. DHHS. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0-. Accessed April 2023;
2. Gandhi R, et al. *JAMA 2022*

Pivotal Trials Informing First-Line Therapy

	HIV RNA <50 Copies/mL (%)
SPRING-2	
Dolutegravir + FTC/TDF or ABC/3TC (n=411)	88
Raltegravir + FTC/TDF or ABC/3TC (n=411)	85
SINGLE	
Dolutegravir + ABC/3TC (n=414)	88
Efavirenz/FTC/TDF (n=419)	81
FLAMINGO	
Dolutegravir + FTC/TDF or ABC/3TC (n=242)	90
Darunavir/r + FTC/TDF or ABC/3TC (n=242)	83
ARIA	
Abacavir/Dolutegravir/Lamivudine (n=248)	82
Atazanavir/r + FTC/TDF (n=247)	71

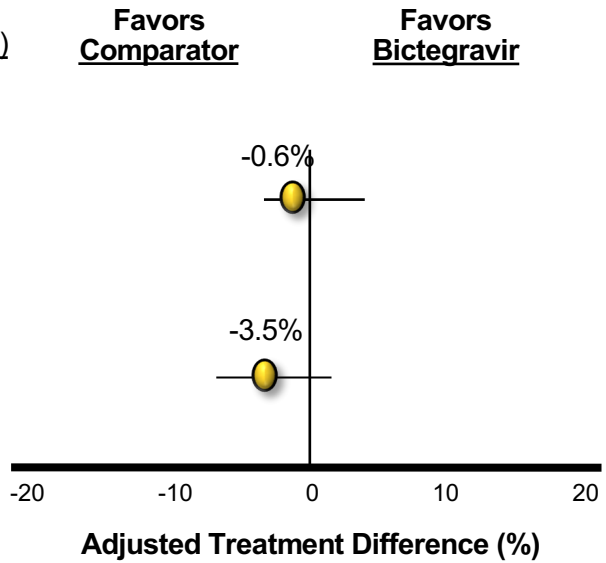


No Resistance Selected for Any Dolutegravir-Based Regimen

Raffi F, et al. *Lancet*. 2013;381:735-743.
Walmsley S, et al. *N Engl J Med*. 2013;369:1807-1818.
Clotet B, et al. *Lancet.* 2014;383:2222-2231.
Orrell C, et al. *Lancet HIV.* 2017;4:e536-e546.

Pivotal Trials Informing First-Line BIC/FTC/TAF Therapy

	HIV RNA <50 Copies/mL (%)
Study 1489	
Bictegravir/FTC/TAF (n=314)	92
Dolutegravir/ABC/3TC (n=315)	93
Study 1490	
Bictegravir/FTC/TAF (n=320)	89
Dolutegravir + FTC/TAF (n=325)	93

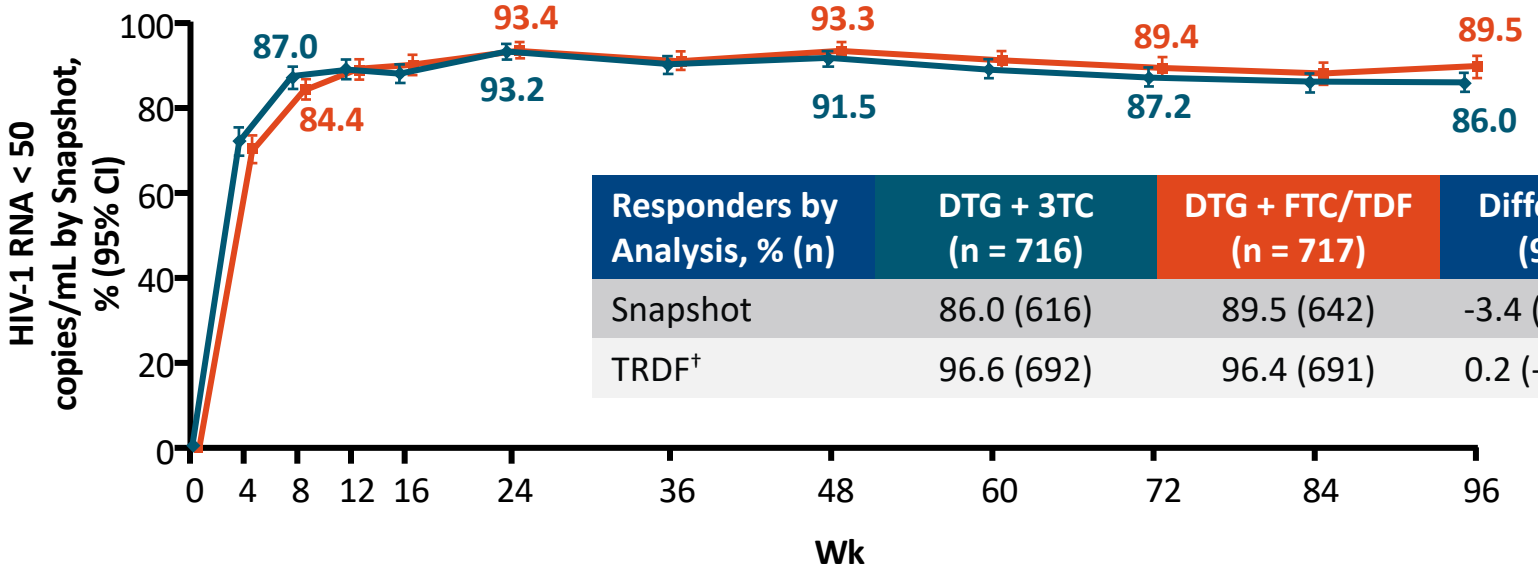


No Resistance Selected for Any Bictegravir- or Dolutegravir-Based Regimen

Gallant J, et al. *Lancet.* 2017;390:2063-2072.
Sax PE, et al. *Lancet.* 2017;390:2073-2082.

GEMINI-1 and -2: Virologic Response at Wk 96

- DTG + 3TC met Snapshot criteria for **noninferior efficacy** vs DTG + FTC/TDF at Wk 96



Responders by Analysis, % (n)	DTG + 3TC (n = 716)	DTG + FTC/TDF (n = 717)	Difference, % (95% CI)
Snapshot	86.0 (616)	89.5 (642)	-3.4 (-6.7 to 0)*
TRDF†	96.6 (692)	96.4 (691)	0.2 (-1.8 to 2.2)

*Adjusted for baseline HIV-1 RNA, baseline CD4+ cell count, and study.
†Accounts for CVW, withdrawal for lack of efficacy or treatment-related AE, and participants meeting protocol-defined stopping criteria.

Cahn. IAS 2019. Abstr WEAB0404LB.

Antiretroviral Guidelines: First-line Therapy

DHHS (1/2023) Recommended for Most People With HIV
Bictegravir/Emtricitabine/Tenofovir alafenamide
Dolutegravir/Abacavir/Lamivudine*
Dolutegravir + Emtricitabine/Tenofovir alafenamide (or disoproxil fumarate)
Dolutegravir/Lamivudine†

*Only for persons HLA-B*5701 negative and without chronic HBV coinfection.
†Not for persons with pre-treatment HIV RNA >500K copies/mL or known to have active HBV coinfection, or no genotype available

IAS-USA (10/2022) Recommended Initial Regimens
Bictegravir/Emtricitabine/Tenofovir alafenamide
Dolutegravir + Emtricitabine/Tenofovir alafenamide (or disoproxil fumarate), or Lamivudine + Tenofovir disoproxil fumarate
Dolutegravir/Lamivudine*

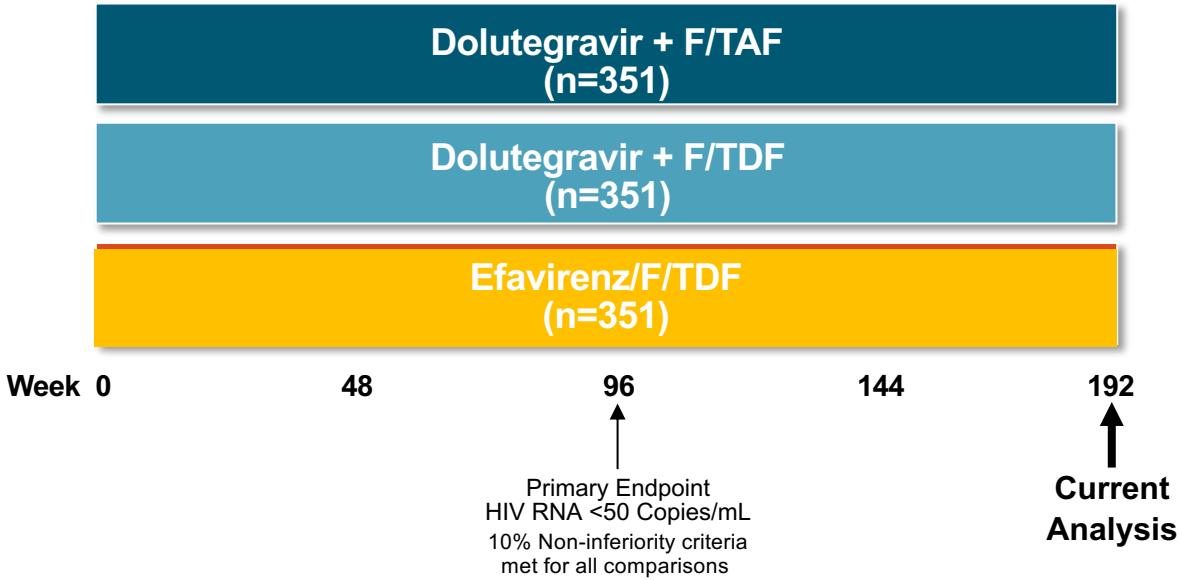
*Not recommended for rapid start because baseline laboratory evaluation results must be reviewed before initiation. Also not recommended for patients with chronic HBV or HIV RNA level >500K copies/mL.
Close monitoring for adherence and virological response is needed.
Not recommended for patients being treated for an active opportunistic infection.

DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf. Revision January 20, 2023.
Gandhi R, et al. JAMA. 2022;324:1651-1669.

ADVANCE: First-line DTG/FTC/TAF vs DTG/FTC/TDF vs EFV/FTC/TDF

Phase 3 (South Africa)

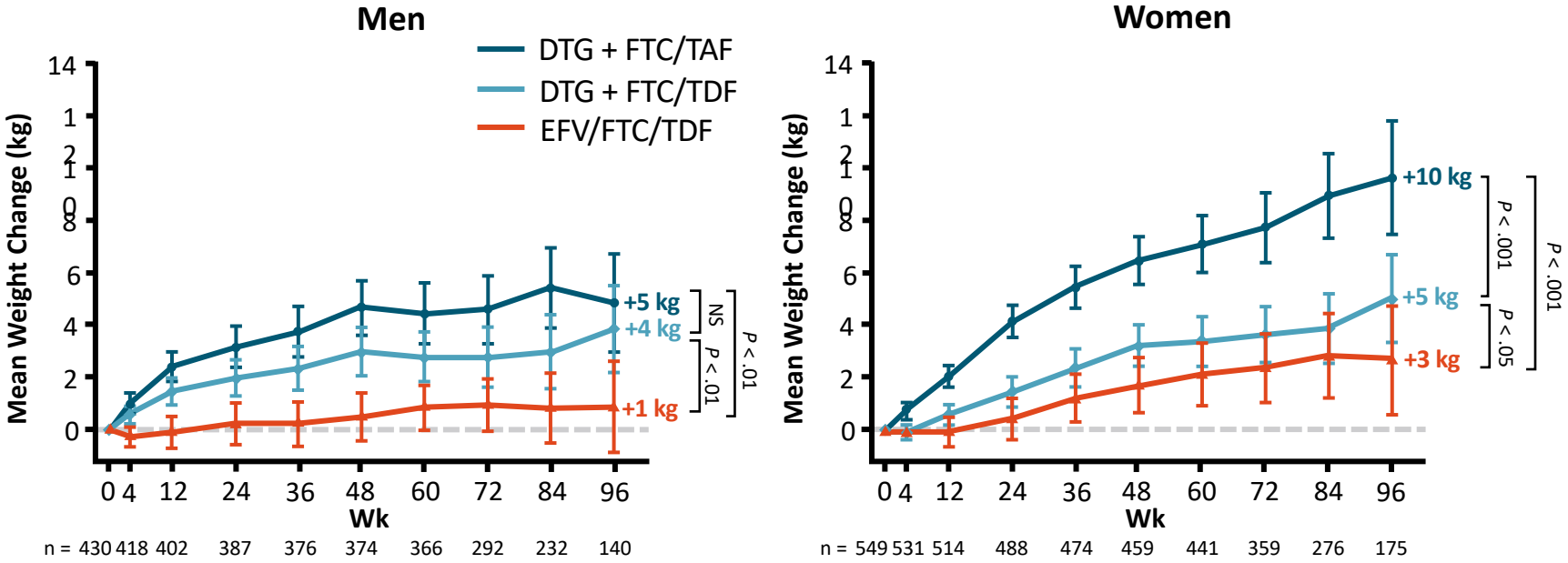
Open-label
Treatment-naïve
HIV RNA ≥500 copies/mL
No TB or pregnancy
No baseline genotyping



Venter. NEJM. 2019; Venter AIDS 2022, Abst PELBB01

ADVANCE: Mean Change in Weight to Wk 96 by Sex

- Significantly greater weight increase* with DTG vs EFV, with TAF vs TDF; plateauing in weight gain after Wk 48 observed in men but not in women

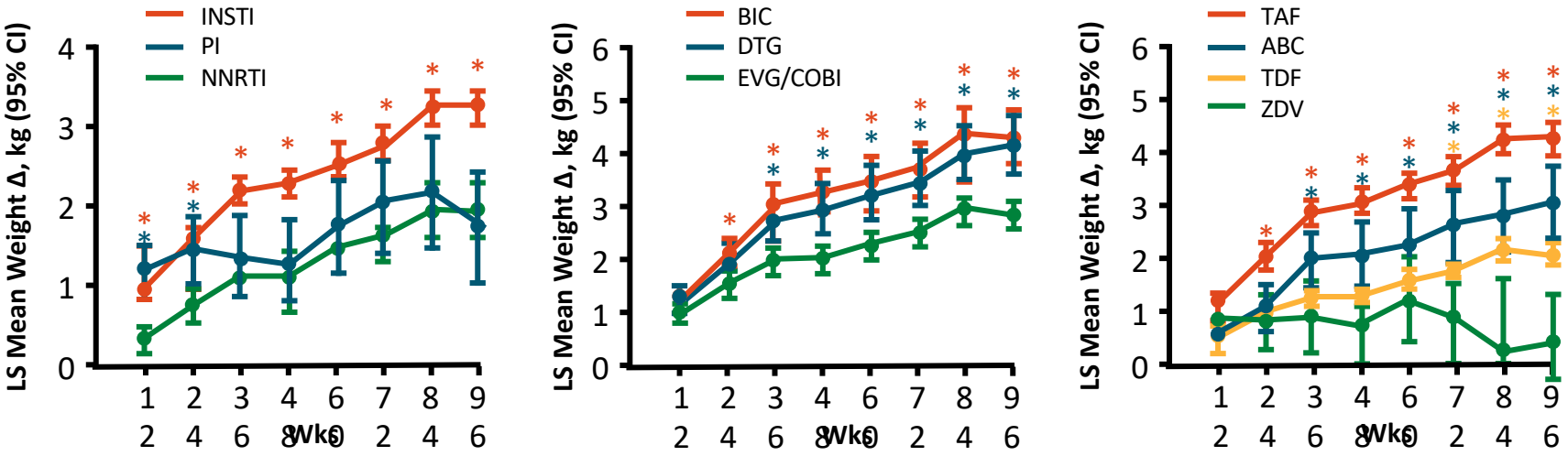


Hill. IAS 2019. Abstr MOAX0102LB.

*Wilcoxon rank-sum comparison at Wk 96.

Multivariate Analysis of Weight Gain Following ART Initiation

- Pooled analysis of weight gain across 8 randomized phase III clinical trials of first-line ART initiation occurring in 2003-2015 (N = 5680)



*Color-coded to match respective comparators, denoting $P \leq .05$ vs NNRTI (first panel), EVG/COBI (second panel), or ZDV (last panel).

Sax. Clin Infect Dis. 2019

Factors to consider when addressing potential weight gain associated with starting ART

- Weight gain occurs in most people starting ART
- Weight gain is potentially greater with 2nd generation INSTIs and TAF
- Weight gain potentially attenuated with EFV and TDF
- There are clear clinical advantages to starting 2nd generation INSTIs over alternative agents and they remain preferred options for most
- The mechanism behind differences in weight gain by ARVs remain poorly understood
- There is no definitive strategy for managing excessive weight gain that may be mediated by select ARVs

Optimization/Simplification of Therapy: Applies to those virologically suppressed

Why

- Simplify regimen (pill number and frequency)
- Tolerability
- Comorbidity
- Drug–drug and drug–food interactions
- Pregnancy
- Cost

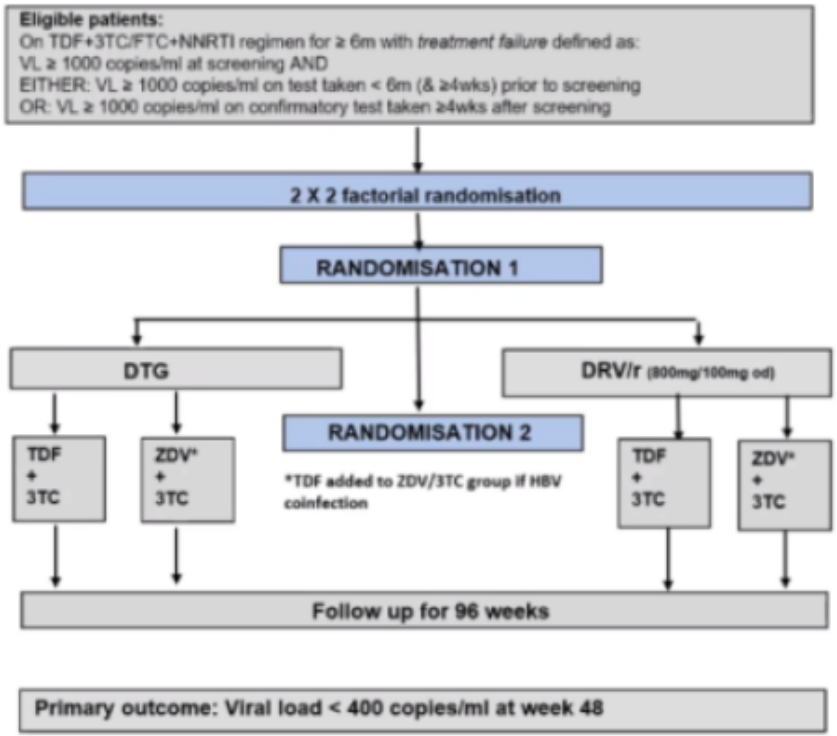
How

- Maintain viral suppression to avoid resistance
- Need to consider
  - Previous ART
  - Previous resistance
  - Likelihood of adherence
  - Drug–drug or drug–food interactions
  - Comorbid conditions

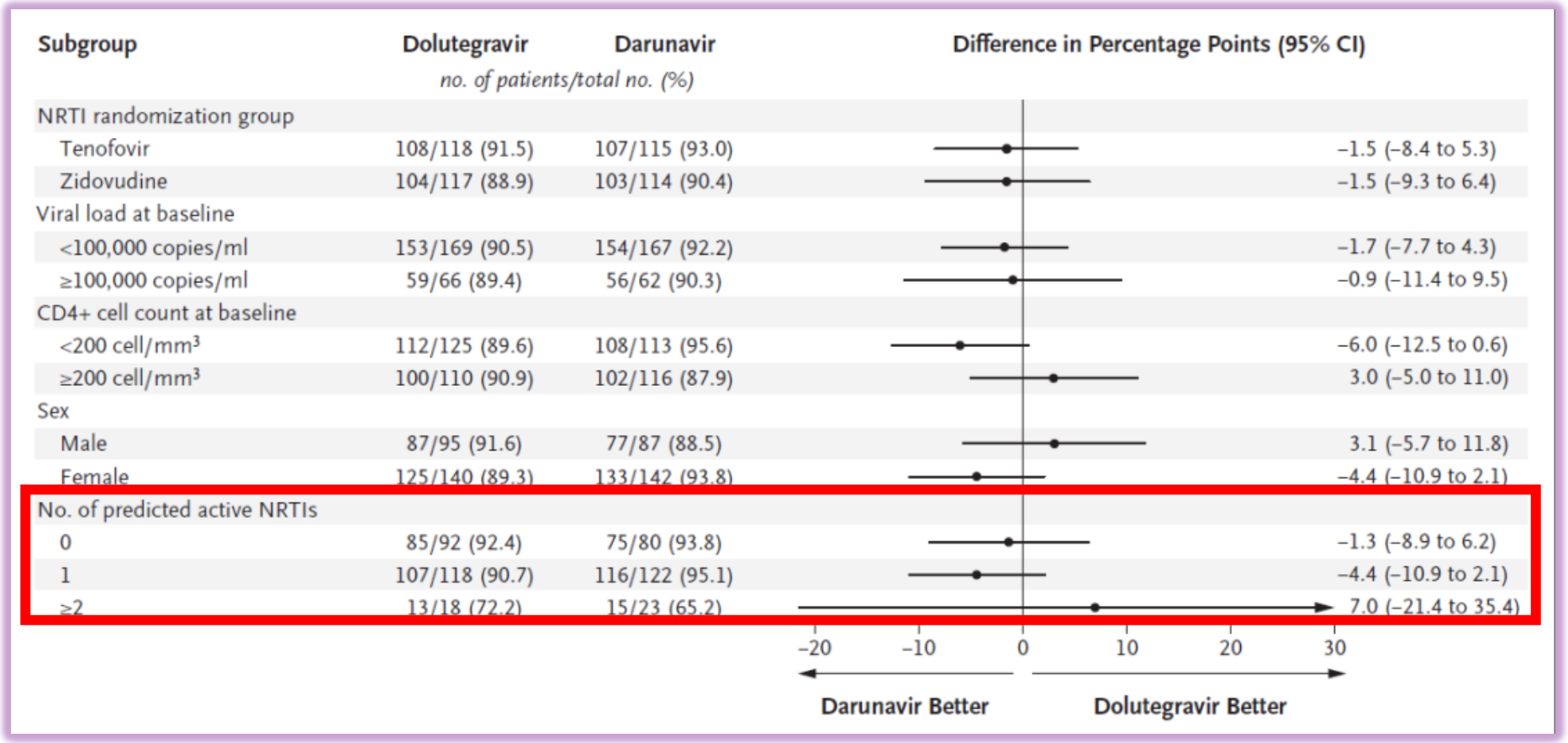
DHHS guidelines. September 2022.

Dolutegravir or Darunavir in Combination with Zidovudine or Tenofovir to Treat HIV

Nicholas I. Paton, M.D., Joseph Musaazi, M.Sc., Cissy Kityo, Ph.D., Stephen Walimbwa, M.D., Anne Hoppe, Ph.D., Apolo Balyegisawa, M.D., Arvind Kaimal, M.D., Grace Mirembe, M.Med., Phionah Tukamushabe, R.N., Gilbert Ategeka, M.D., James Hakim, F.R.C.P., Henry Mugerwa, M.D., Abraham Siika, M.Med., Jesca Asienzo, B.P.L.M., Barbara Castelnuovo, Ph.D., Agnes Kiragga, Ph.D., and Andrew Kambugu, M.Med., for the NADIA Trial Team*



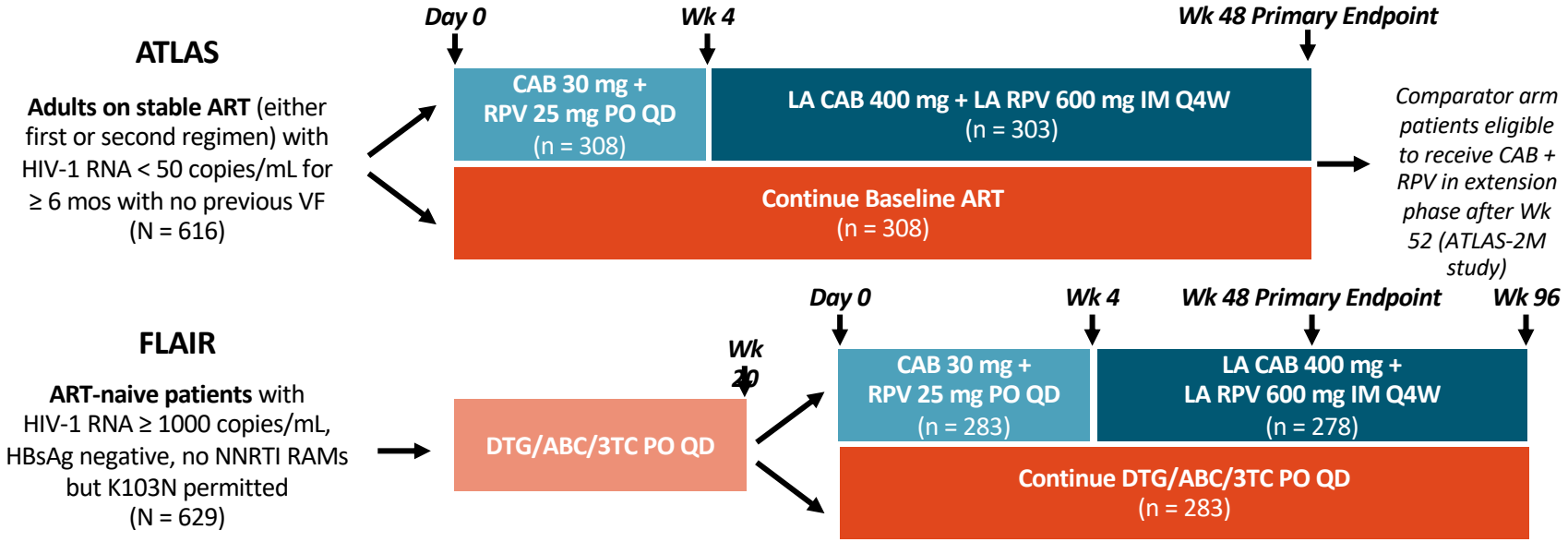
Paton N, et al. NEJM 2021; 385:330-341



Paton N, et al. NEJM 2021;
385:330-341

ATLAS and FLAIR: LA CAB + RPV Q4 weeks vs. Baseline ART

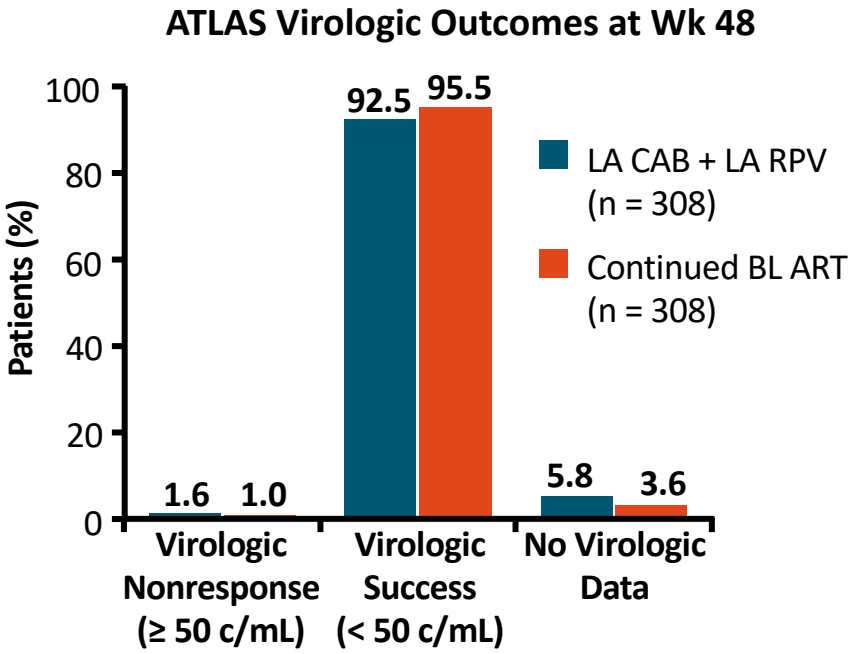
- Multicenter, randomized, open-label phase III noninferiority trials

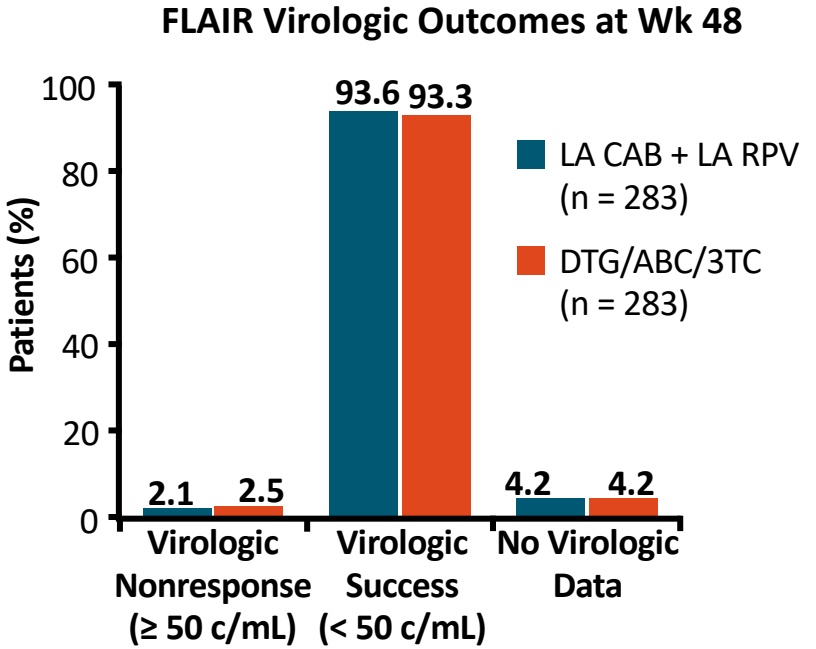


- Primary endpoint for both trials: HIV-1 RNA ≥ 50 copies/mL at Wk 48 by FDA Snapshot in ITT-E

1. Swindells. NEJM. 2020;382:1112. 2. Orkin. NEJM. 2020;382:1124.

ATLAS and FLAIR: LA CAB + RPV Q4 weeks vs. Baseline ART





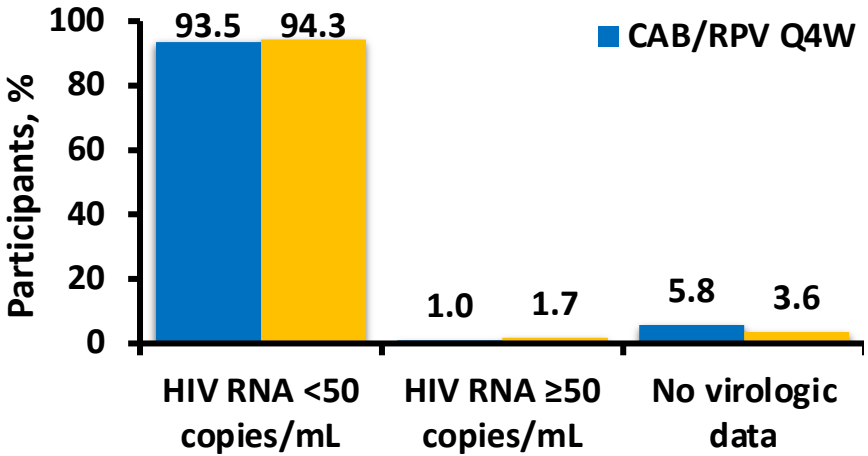
- Noninferiority also observed at Wk 96
- No additional CVF during Wk 48 to 96 in CAB+RPV arm

Swindells. NEJM. 2020;382:1112.

Orkin. NEJM. 2020;382:1124. Orkin. CROI 2020. Abstr 482LB.

Long-Acting CAB/RPV Q4W vs Q8W
ATLAS-2M (Wk 48)

CAB/RPV Q8W noninferior to Q4W

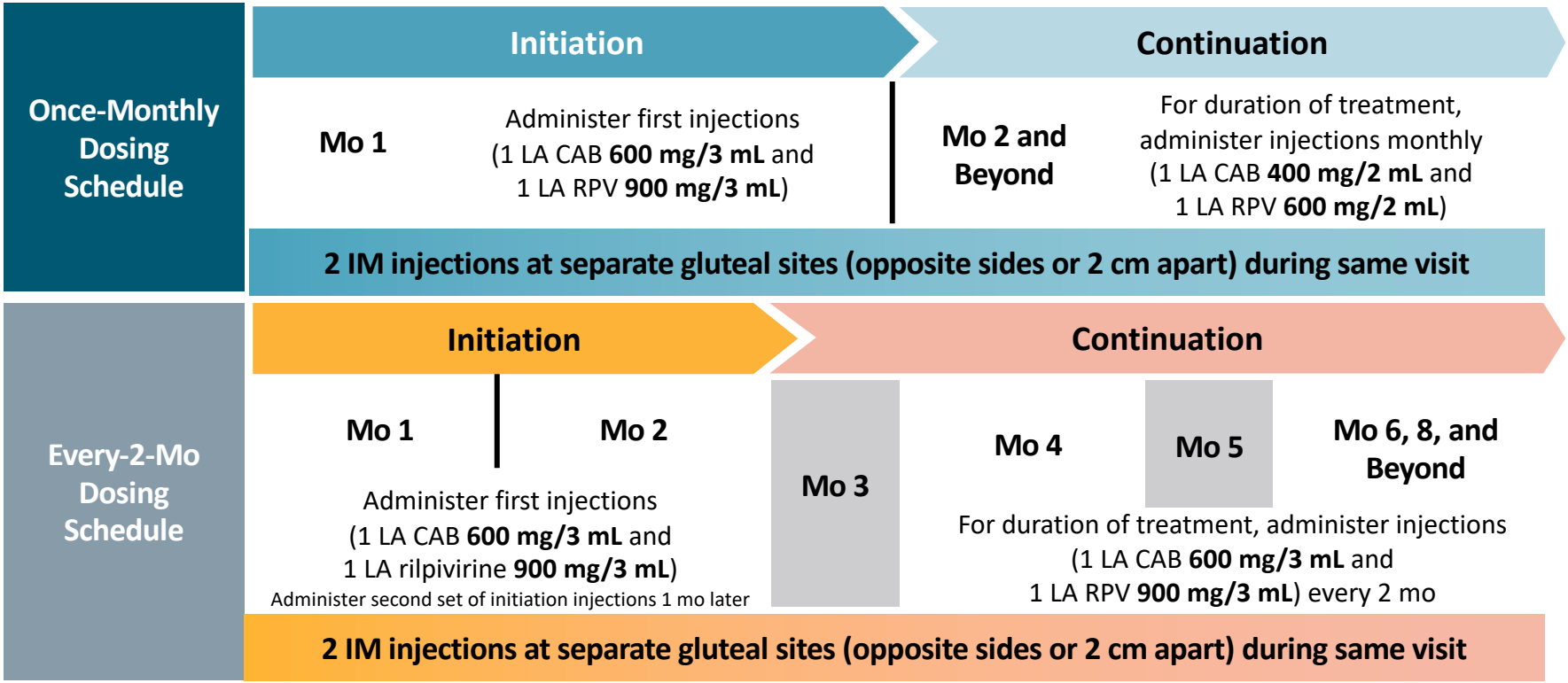


- Injection site reactions were rated as mild-to-moderate by 98% of participants experiencing them
  - Median duration of 3 days

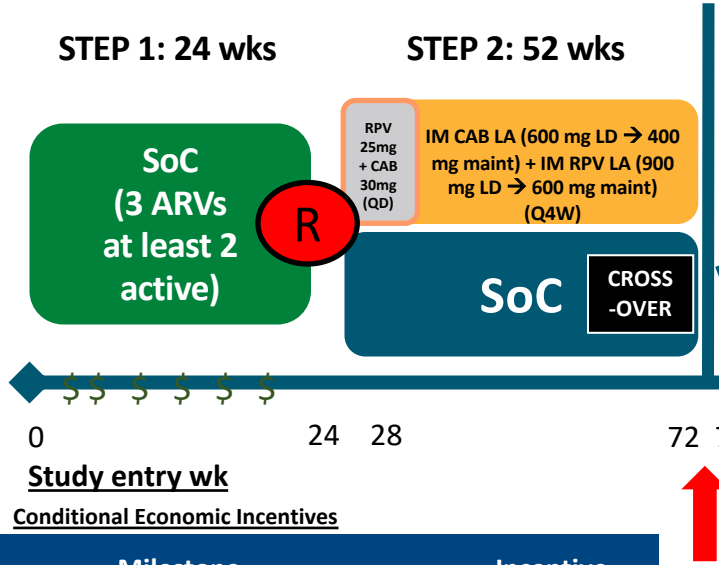
Only indicated for those virologically suppressed
Limited data in those with concern for or actual poor adherence with visits or therapy

Jaeger et al. Lancet HIV 2021: e679-689

LA CAB + RPV: Getting Started and Follow-up



ACTG 5359: Long-acting Cabotegravir + Rilpivirine in Persons With HIV Nonadherent to Current ART



Conditional Economic Incentives

Step 1, Wk	Milestone	Incentive
2	Completed visit	$75
4	HIV-1 RNA > 1 $\log_{10}$ drop	$75
8	HIV-1 RNA > 2 $\log_{10}$ drop	$75
12	HIV-1 RNA < 200 copies/mL	$150
16	HIV-1 RNA < 200 copies/mL	$150
20	HIV-1 RNA < 50 copies/mL	$150

LA CAB + RPV: SF Ward 86

- LA CAB + RPV using protocol with biweekly patient review and extensive wrap around services
- LA CAB + RPV inclusion criteria:
  - Viral suppression **not required**
  - No RPV or INSTI mutations
  - Agree to Q4 week clinic visits and to provide contact information for outreach from staff
- 133 PWH initiated LA CAB + RPV June 2021 - November 2022

Characteristic, n (%)	**LA CAB + RPV (N = 133)**
Race/ethnicity	
▪ Black	21 (16)
▪ Latinx	50 (38)
▪ Multiracial	19 (14)
Unstable housing	77 (58)
Homeless	11 (8)
Medicare/Medicaid	130 (98)
Current stimulant use	44 (33)
Major mental illness	51 (38)
Viremic (HIV-1 RNA >30 c/mL)	**57 (43)**

Of those viremic, mean HIV-1 RNA: 4.21 $\log_{10}$, median CD4 cell count: 215 cells/mm^3

Gandhi M, et al. Ann Intern Med 2023; 176: 969-974

War 86 Virologic Outcomes With LA CAB + RPV

- On-time injections: 74%
- Suppressed at entry (n=76)
  - 100% (95% CI: 94, 100) without viral rebound
- Viremic at entry (n=57)
  - 55 achieved suppression at median of 33 days
  - 2 with virologic failure, both in <24 weeks, both with minor resistance mutations pre-entry and <2 log decline at first visit
    - Patient 1: V179I BL and developed Y181C, L100I
    - Patient 2: T97A BL and developed R263K, E138K
  - Subsequently protocol excluded those with any resistance at BL

Gandhi M, et al. Ann Intern Med 2023; 176: 969-974

DOR/ISL (100/0.75 mg) vs BIC/FTC/TAF as First-line Treatment of HIV: Study Design and Results

- Double-blind, randomized phase III trial

Stratified by HIV-1 RNA </≥100,00 and CD4+ cell count </≥200

48 wk *96 wk*

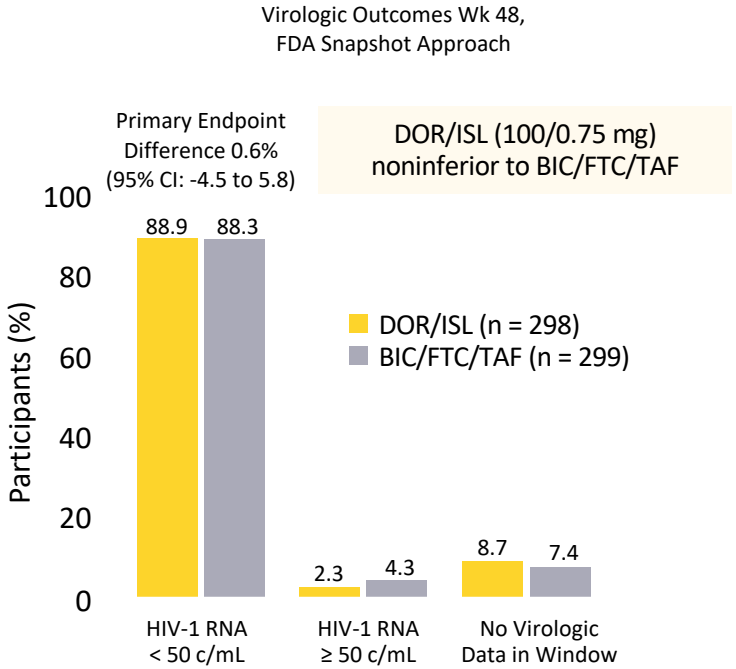
Adults with HIV-1 RNA ≥500 c/mL; not previously treated with ART; without virologic resistance* and HBV† (N = 597)

DOR/ISL (100/0.75 mg) PO once daily (n = 298)

BIC/FTC/TAF PO once daily (n = 299)

168 wk

*V106A/M, V108I, Y188I, H221Y, P225H, F227C/L, M230I/L, L234I, P236L, Y318F, K65R/E/N, M184I/V, K70E, T69insert, Q151M, or ≥3 of M41L, D67N, K70R, L210W, T215F/Y, K219E/Q.
†HCV without synthetic hepatic dysfunction allowed.



- Primary endpoint: HIV-1 RNA <50 c/mL at Wk 48 by FDA snapshot analysis
- BL characteristics: 25% female, 20% CD4 count <200 cells/mm^3, 19% HIV-1 RNA >100,000 c/mL

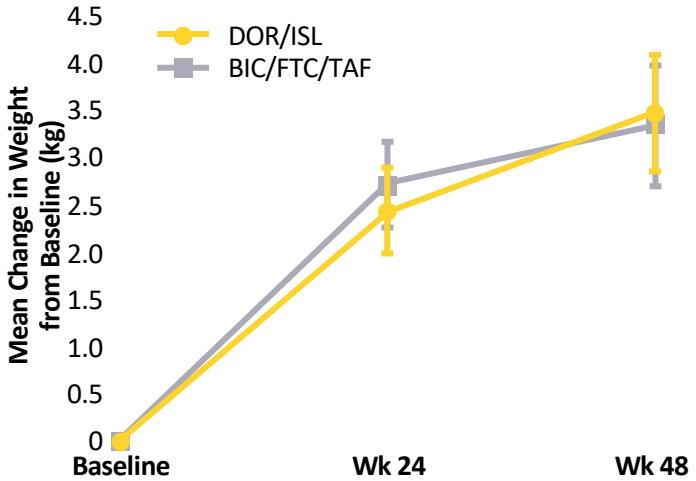
Rockstroh. IAS 2023. Abstr OALBX0102.

DOR/ISL (100/0.75 mg) vs BIC/FTC/TAF as First-line Treatment of HIV: Virologic Failure and AEs

Protocol-Defined Virologic Failure

Arm	Wk	VF	Treatment-Emergent RASs	Phenotype
DOR/ISL	24	Incomplete response	**NNRTI: V106A, P225H NRTI: M184I**	**R: DOR**
BIC/FTC/TAF	8	Rebound	None	S: FTC/TAF
BIC/FTC/TAF	36	Rebound	No result	Unavailable
BIC/FTC/TAF	24	Incomplete response	None	S: BIC/FTC/TAF
BIC/FTC/TAF	36	Incomplete response	None	S: BIC/FTC/TAF

- Similar rates of AEs and serious AEs
  - DOR/ISL associated with numerically higher rates of lymphocyte count decrease, including requiring treatment discontinuation; similar rates of infection-related AEs



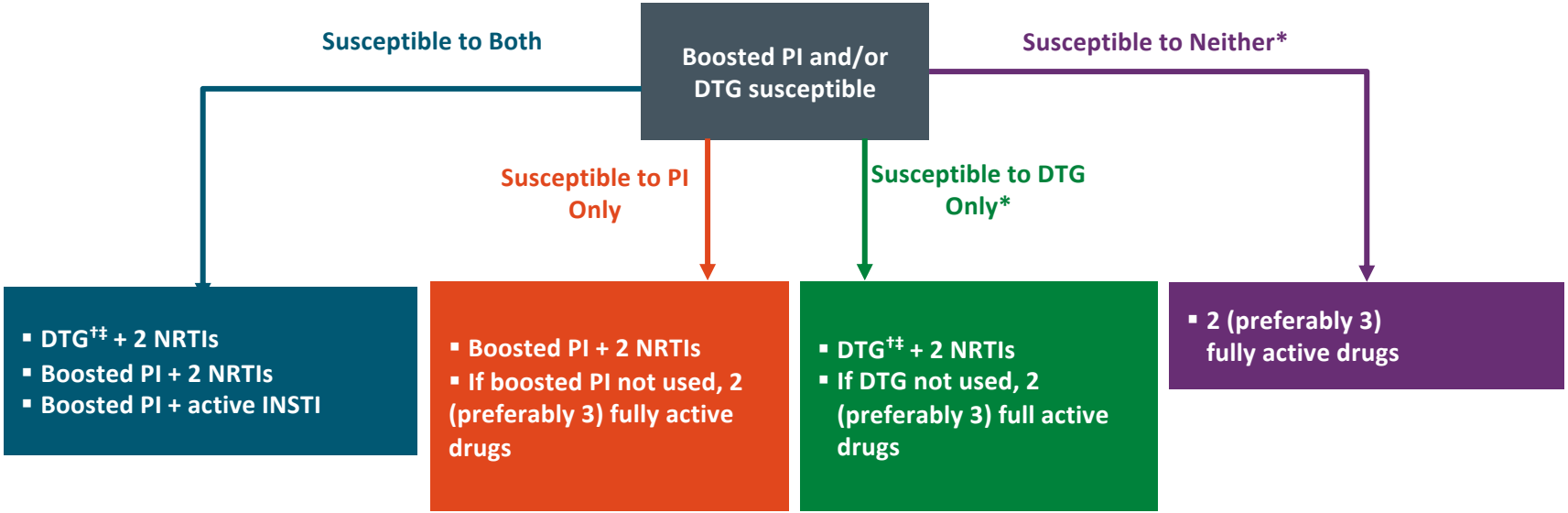
- **No difference in mean change in weight**
  - DOR/ISL: +3.45 kg (95% CI 2.83-4.06)
  - BIC/FTC/TAF: +3.32 kg (95% CI 2.86-3.96)

DOR/ISL at lower dose (100/0.25 mg) moving forward in development

Rockstroh. IAS 2023. Abstr OALBX0102.

Managing Antiretroviral Failure

Management of ARV Failure: Second Line and Beyond



*Rare in patients never exposed to unboosted PIs (eg, NFV, DHHS alternative since 2003 and not recommended since 2008).
†If INSTI naive or experienced with no resistance (limited data in patients with resistance to RAL or EVG but susceptibility to DTG).
‡Data limited to DTG, but similar results might be seen with BIC.

Adapted from DHHS ART Guidelines. January 2022.

Ibalizumab: Virologic Outcomes (Wk 96)

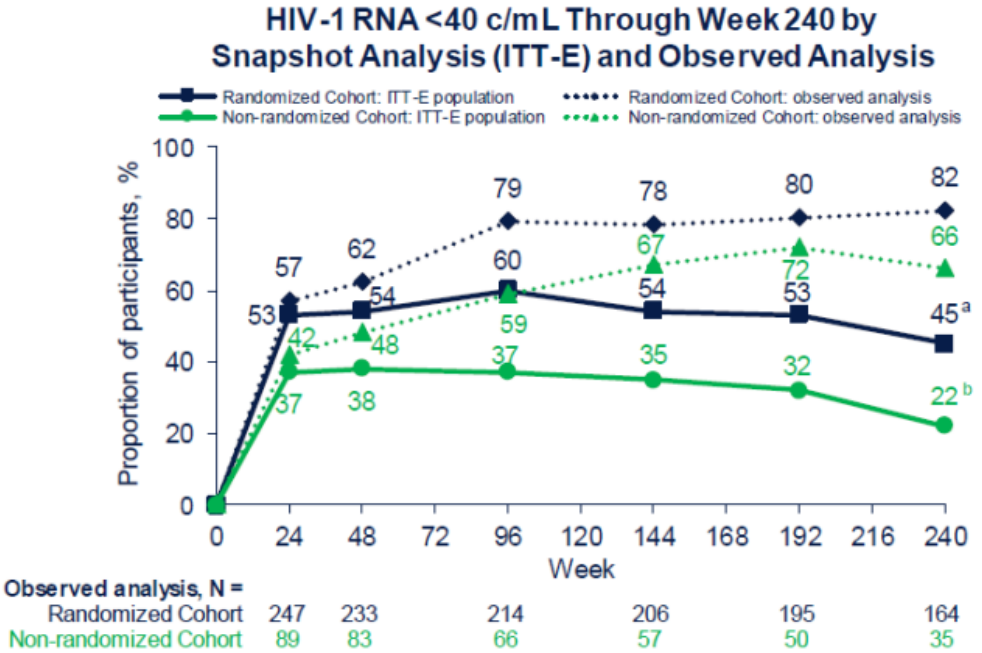
- TMB-311: patients enrolled in US and Puerto Rico who completed 25 wks in TMB-301 continued ibalizumab 800 mg Q2W for up to 96 wks

Virologic Outcome	Day 14[1] (N = 40)	Wk 25[1] (N = 40)	Wk 48[2,3] (N = 27)	Wk 96[4] (N = 27)
≥ 0.5 log_{10} HIV-1 RNA decrease, %	83*†	63	NR	NR
≥ 1.0 log_{10} HIV-1 RNA decrease, %	60	55	67	NR
Mean log_{10} HIV-1 RNA decrease	1.1	1.6	2.1	NR
Median log_{10} HIV-1 RNA decrease	NR	2.5	2.8	2.8
HIV-1 RNA < 50 copies/mL, %	NR	43	59	56
HIV-1 RNA < 200 copies/mL, %	NR	50	63	NR

1. Emu. NEJM. 2018;379:645. 2. Emu. IDSA 2017. Abstr 1686. 3. Emu. HIV Glasgow 2018. Abstr O345.
4. Emu. CROI 2019. Abstr 485. 5. DeJesus. HIV Glasgow 2018. Abstr P064.

Fostemsavir: Virologic Outcomes (Wk 240)

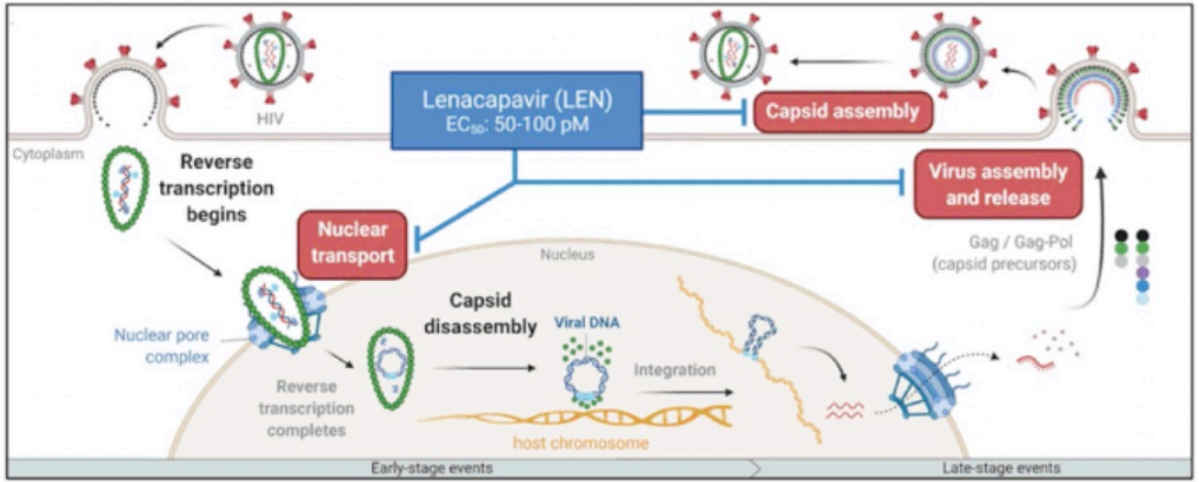
- In the Randomized Cohort, virologic response rates (HIV-1 RNA <40 c/mL) generally remained consistent through Week 240
  - Reduced virologic response rates by Snapshot at Week 192 and beyond were partially confounded by missing data due to COVID-19: at Week 240, 19 (7%) participants in the Randomized Cohort and 5 (5%) in the Non-randomized Cohort were counted as virologic failures for this reason



ITT-E participants without an HIV-1 RNA value at the relevant time point or those who changed OBT due to lack of efficacy up to each time point counted as failures.

[a]ITT-E population, N=267. [b]ITT-E population, N=92.

Aberg et al. AIDS 2022; Virtual and Montreal, Canada. Poster EPB16



Link JO, et al. Nature 2020;584:614-8; Bester SM, et al. Science 2020;370:360-4.

Lenacapavir
Dec 2022
approved for
Q6M SC

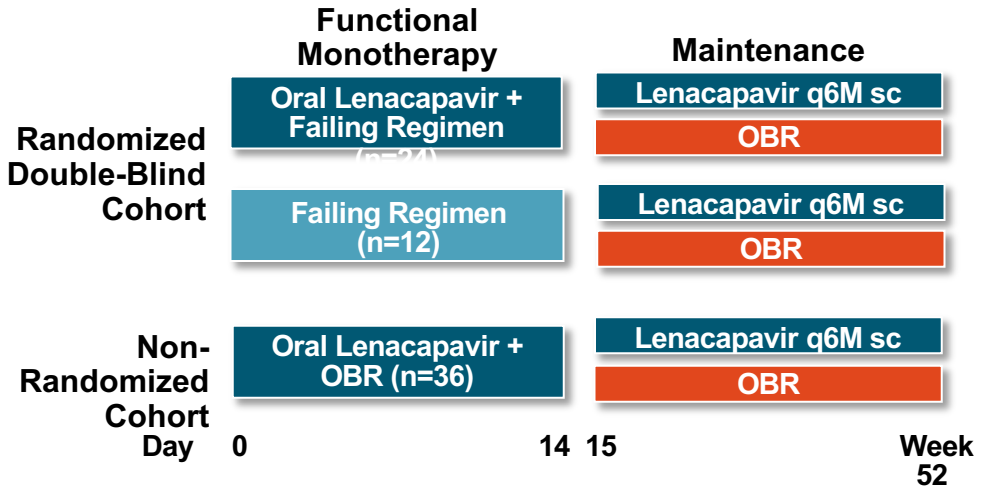
- Two 22 g, 0.5 inch SC injections q6 months by health care provider
- SC abdominal injection with each 2 inches from navel (rotate injection sites)
- Contraindicated with strong CYP3A inducers
- Insufficient human data for use during pregnancy

fda.gov/news-events/press-announcements/fda-approves-new-hiv-drug-adults-limited-treatment-options.
Lenacapavir extended-release injectable solution PI. Updated December 2022.

CAPELLA Study: Phase 3, LEN in Highly Treatment Experienced Patients

Treatment-experienced on failing regimen
Resistance to ≥2 agents from
3 of 4 main ARV classes
≤2 fully active agents available

Non-randomized cohort
Pre-randomization repeat HIV RNA
Decline of ≥0.5 $\log_{10}$ copies/mL or <400 c/mL



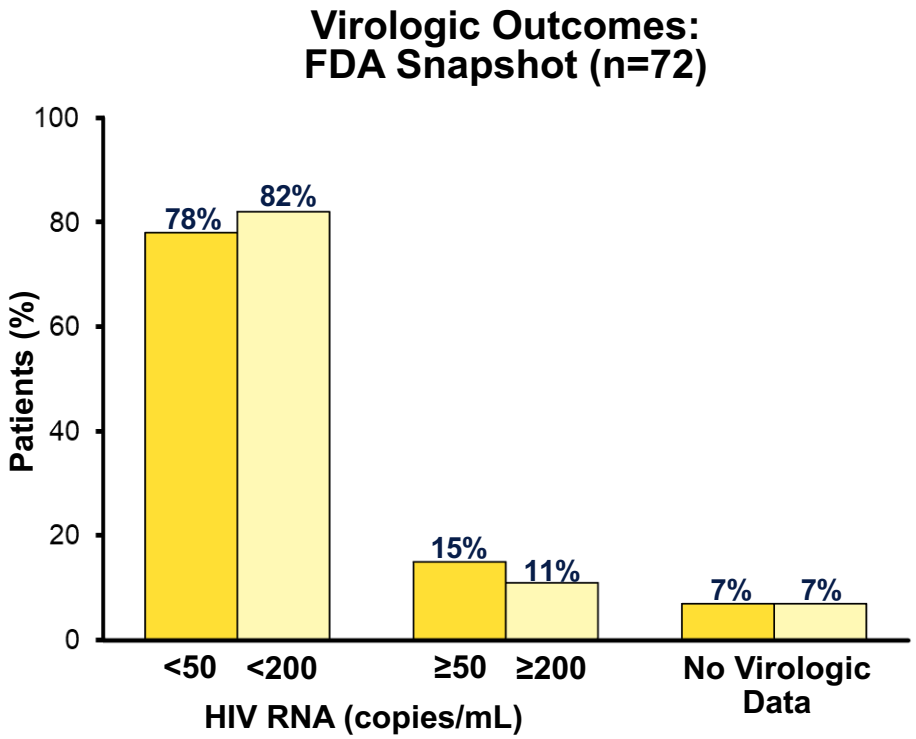
- Oral LEN 600 mg day 1 and 2, 300 mg on day 8.
- SC LEN 927 mg (2 x 1.5 mL) day 15 and q6 months.
- Primary outcome (randomized cohort):
  ≥0.5 $\log_{10}$ copies/mL decline after 14 days.

Baseline resistance:
NRTI: 99%.
NNRTI: 97%.
PI: 81%.
INSTI: 69%.
All 4 major drug classes: 46%.

Segal-Maurer et al. NEJM 2022; 386:1793-1803

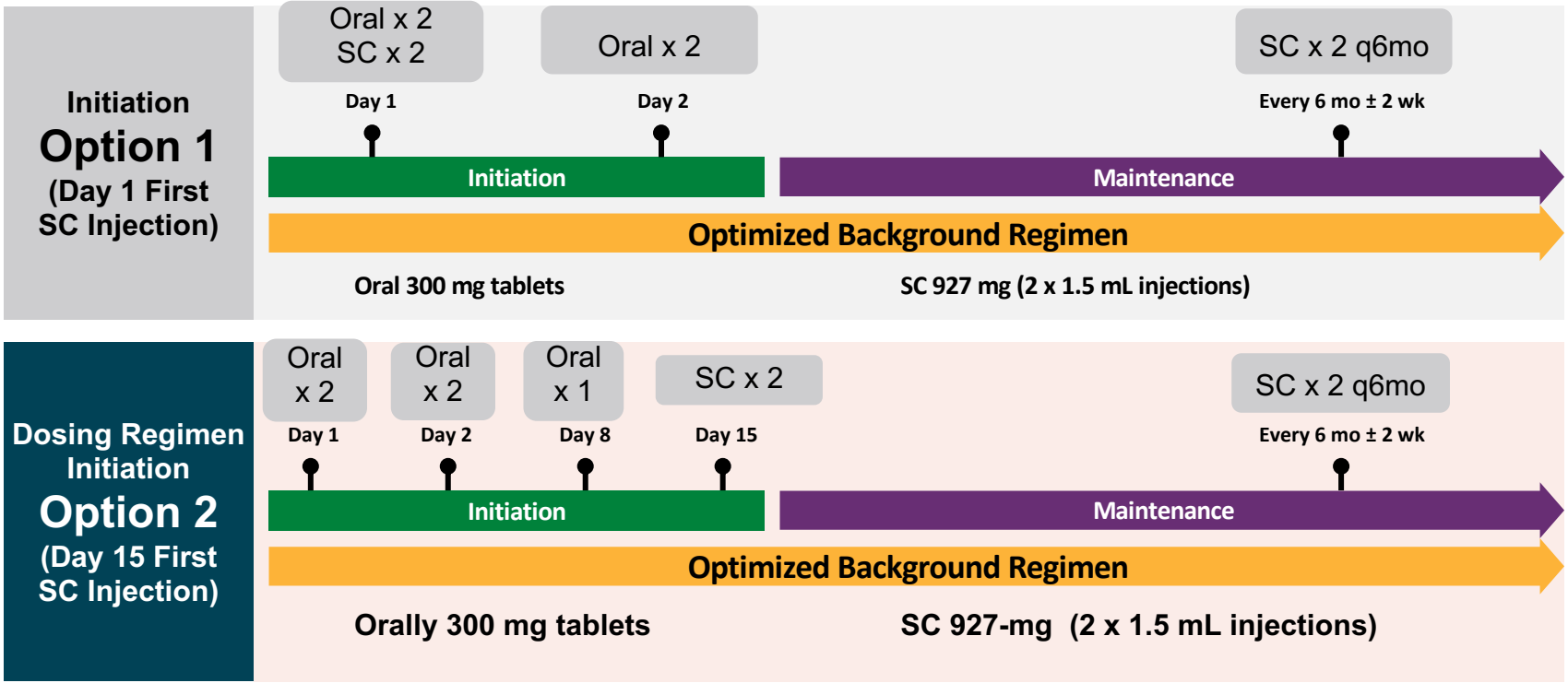
CAPELLA Study: Outcomes Week 52

- HIV RNA <50 copies by number of active agents in OBR
  - 0 (n=12): 75%; 1 (n=26): 77%; ≥2 (n=34): 79%
- CD4 increase: 84 cells/μL
- LEN resistance (n=9)
  - Resuppressed during receipt of LEN (4/9)
- Tolerability
  - Discontinuations due to injection site reaction (n=1)
  - No serious drug-related adverse events



Segal-Maurer et al. NEJM 2022; 386:1793-1803

Lenacapavir Initiation and Maintenance Schedule

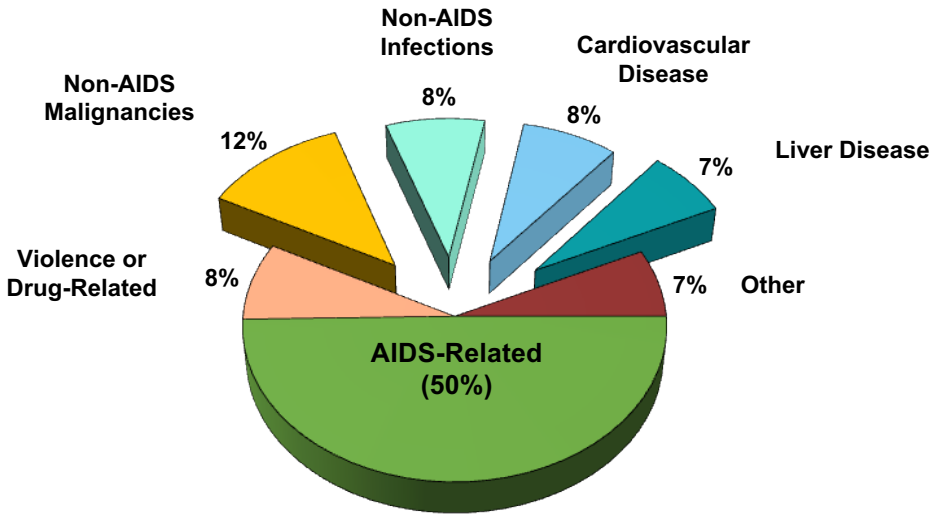


Lenacapavir extended-release injectable solution PI. Updated December 2022.

Healthy Living with HIV

Why do we need more than highly effective treatment?

ART Cohort Collaboration: 50% of Deaths Due to Non-AIDS-Related Causes (1996-2006)



n=39,272 HIV-infected patients from 13 cohort studies in Europe and North America who were treated with ART. Causes of death were retrospectively assigned to 85% of total deaths (1597/1876).

ART Collaboration. *Clin Infect Dis*. 2010;50:1387-1396.

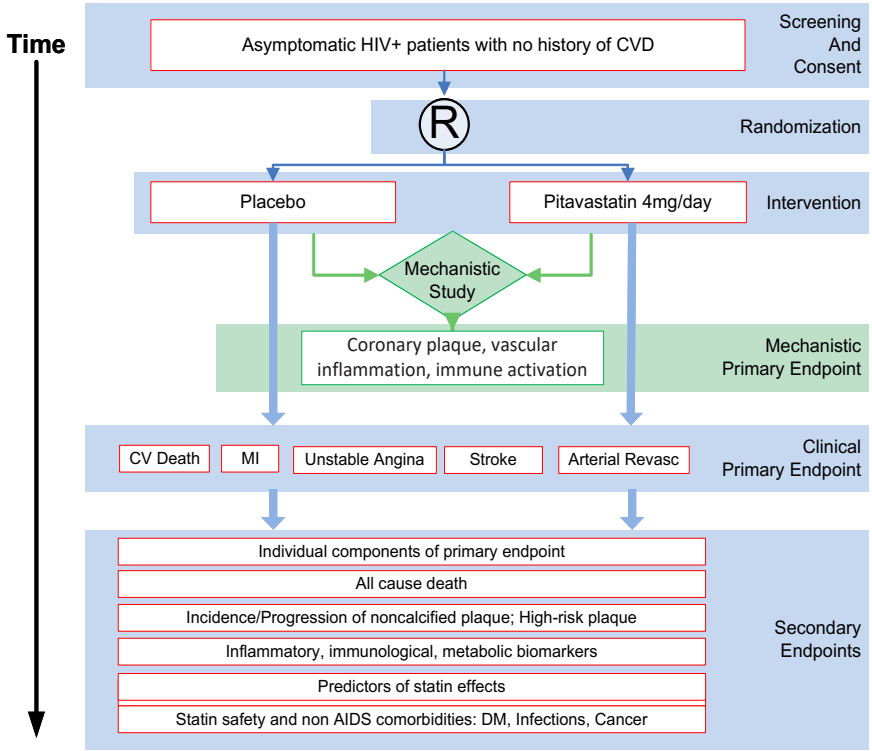
Monitoring

- Depression screening (annually)
- Substance use screening
- BP and weight every visit
- STI screening (q3-6 months)
- HCV annually (sexually active MSM)
- TB screening annually in those at risk
- BMD annually (men >50 yr/women postmenopausal)
- Cardiovascular
- Frailty assessment (not specified in guidelines)

Thompson M, et al. CID 2020

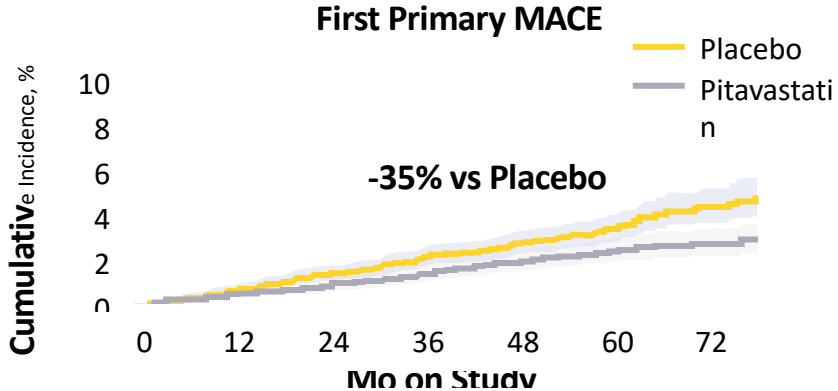
REPRIEVE

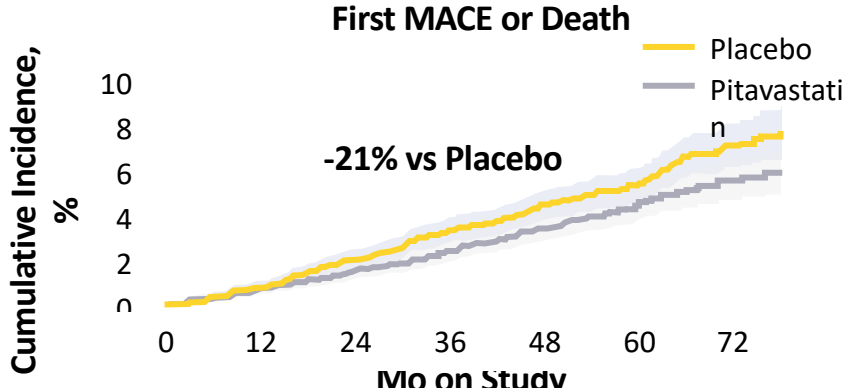
Randomized Trial to Prevent Vascular Events in HIV



REPRIEVE: Time to First Major Cardiovascular Event

- Baseline characteristics well balanced between treatment arms; median ASCVD risk score 4.5% (IQR: 2.1 to 7.0) and median LDL cholesterol 108 mg/dL (IQR 87 to 128)
- Pitavastatin prolonged time to first MACE vs placebo



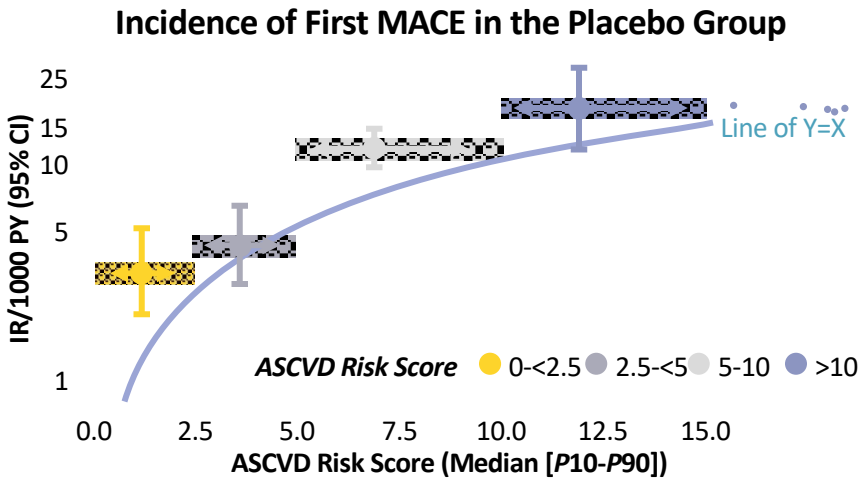


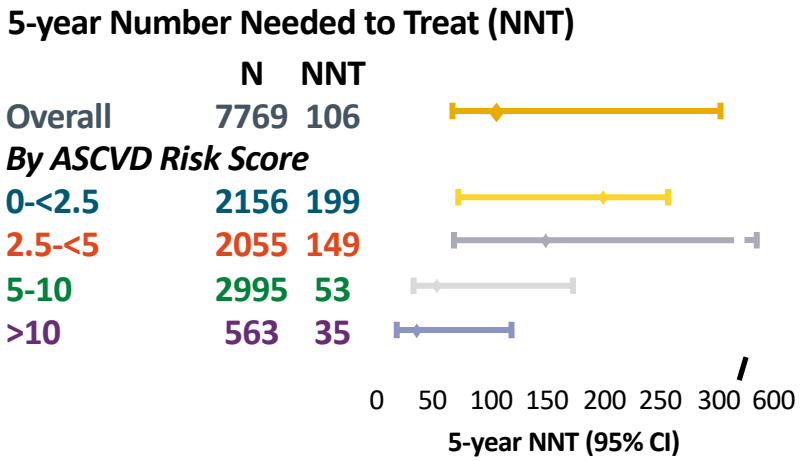
Cumulative incidence of event							
	0%	0.6%	1.0%	1.4%	1.9%	2.4%	2.7%
Patients at Risk, n	0%	0.7%	1.4%	2.1%	2.7%	3.4%	4.4%
Pitavastatin	3888	3647	3475	3364	2997	1947	1052
Placebo	3881	3693	3506	3356	2997	2182	959

Cumulative incidence of event							
	0%	0.8%	1.6%	2.4%	3.4%	4.5%	5.5%
Patients at Risk, n	0%	0.8%	2.0%	3.3%	4.4%	5.3%	7.1%
Pitavastatin	3888	3647	3475	3364	2998	1948	1027
Placebo	3881	3693	3506	3356	2997	1975	919

Grinspoon. IAS 2023. Abstr SY06. Grinspoon. NEJM. 2023;[Epub].

REPRIEVE: First Major Cardiovascular Event By ASCVD Risk Score





- 5-yr NNT of 106 (95% CI: 64-303) compares favorably with a range of 80-160 for HTN treatment in other studies
- Event rates increased with increasing risk categories for ASCVD, suggesting greater benefit among the participants at higher CV risk at baseline

Grinspoon. IAS 2023. Abstr SY06. Grinspoon. NEJM. 2023;[Epub].

Cancer Screening

- Prostate – DRE (55-69 yrs), PSA (shared decision making)
- Colorectal- colonoscopy or FIT (≥45 yrs)
- Breast cancer- mammogram (40-75 yrs- at least every other year)
- Cervical cancer- PAP per guidelines
- Anal cancer- DRE qyr (anal PAP controversial)
- Hepatocellular cancer- US q6 months if cirrhosis
- Low-dose chest CT- 20+ py (50-80 yrs) - stop once quit >15 yrs

Thompson M, et al. CID 2020 with select updates

Vaccination

- Pneumococcus (PCV 13, 20)- if PCV 13, PCV 23 q5 yrs
- Influenza annually
- Tetanus-diptheria (Tdap) and tetanus toxoid or Tdap q10 yrs
- Meningococcal (A, C, W and Y) x 2 doses, booster q5 yr
- Hepatitis A and B if not immune
- HPV if ≤26 yrs, consider if 27-45 yrs
- Mpox x 2 doses
- Varicella zoster x 2 doses (regardless of age)
- COVID-19

Thompson M, et al. CID 2020

Prevention of Respiratory Viral Infections: Influenza, COVID-19 and RSV

Interim estimated effectiveness of 2022-2023 influenza vaccines in the United States:

71%

against symptomatic infection among children

54%

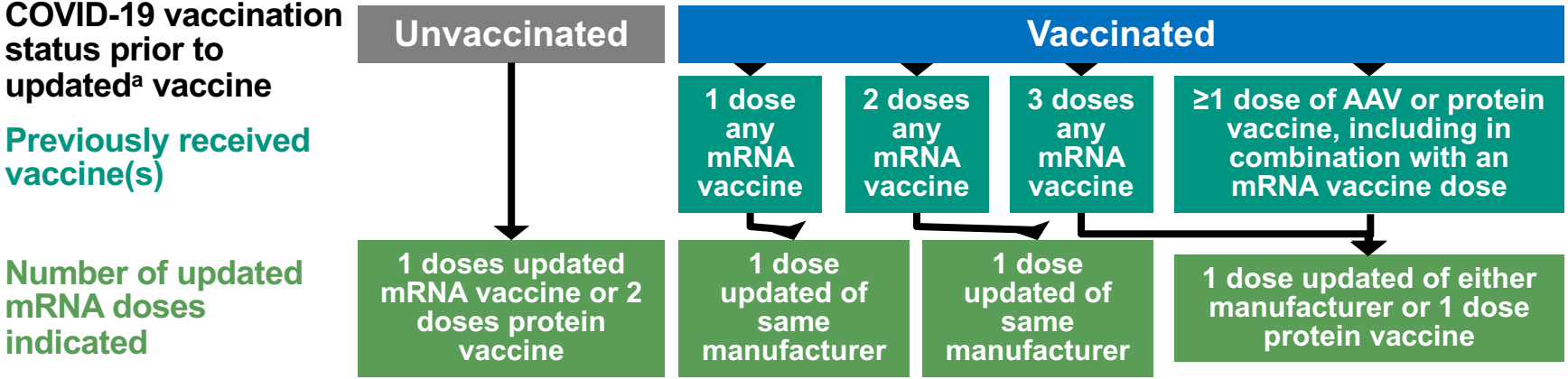
overall among people aged 6 months to 64 years

35%

among adults aged 65 years or older

COVID-19 Vaccine Recommendations for Immunocompetent (≥12 Years)

Updated 2023-2024 Vaccine



The CDC recommends the updated COVID-19 vaccine for everyone aged ≥6 months. This is particularly important for close contacts of immunocompromised patients.

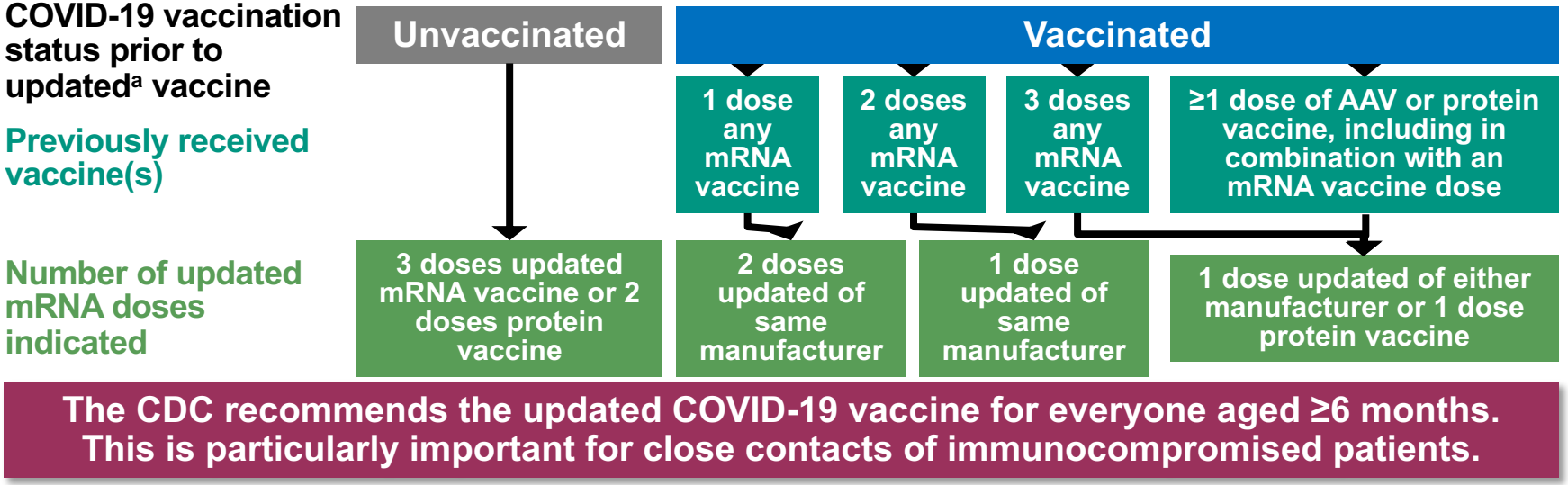
[a]Updated indicates the monovalent 2023-2024 formula targeting the XBB subfamily.

AAV, adeno-associated viral; mRNA, messenger RNA.

CDC. Accessed September 19, 2023. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#table-02.

COVID-19 Vaccine Recommendations for Immunocompromised (≥12 Years)

Updated 2023-2024 Vaccine



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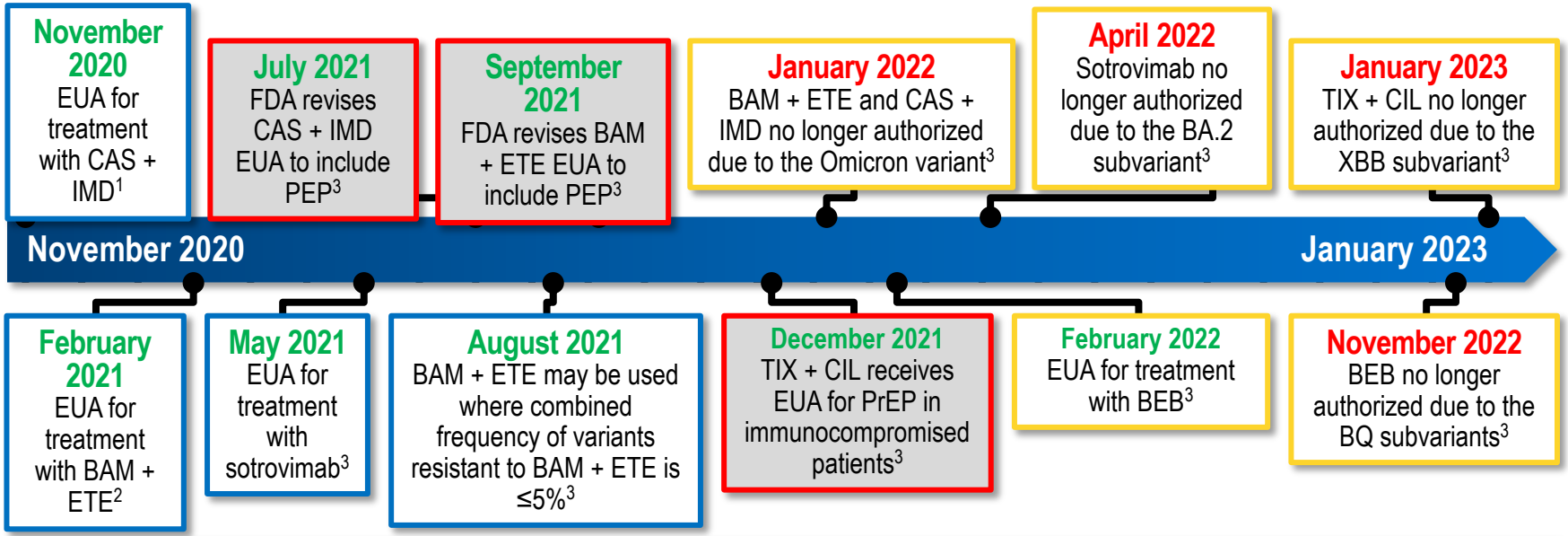
CDC. Accessed September 19, 2023. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#table-02.

History of Anti-SARS-CoV-2 mAb EUAs for High-Risk Patients



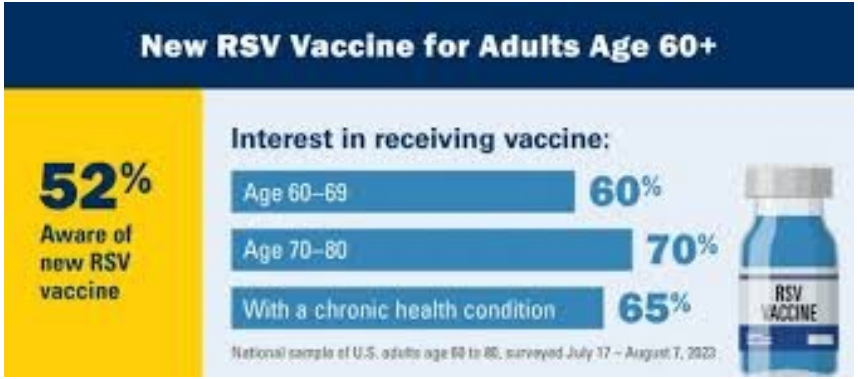
Distribution of anti-SARS-CoV-2 mAbs was often paused or restricted by HHS region as variants and subvariants spread at different rates.

PEP, postexposure prophylaxis; PrEP, pre-exposure prophylaxis.

1. FDA. Accessed August 31, 2023. https://www.fda.gov/media/145610/download; 2. FDA. Accessed August 31, 2023. https://www.fda.gov/media/145801/download; 3. Department of Health and Human Services (DHHS). Accessed August 31, 2023. https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/default.aspx.

Respiratory Syncytial Virus (RSV)

- Two Respiratory Syncytial Virus (RSV) vaccines are approved for people ages 60 years and older
  - Arexvy (GSK adjuvanted RSV vaccine)
  - Abrysvo (Pfizer RSV vaccine)
- CDC recommends that adults ages 60 years and older may receive RSV vaccination, using shared clinical decision-making (SCDM). This means that health care providers should talk to these individuals about whether RSV vaccination is appropriate for them



Conclusions

- Major advances have been made in HIV PrEP and Treatment
- STI PEP represents a potentially important strategy to compliment PrEP and HIV U=U
- Increased focus on strategies to preserve health in those living with HIV on antiretrovirals
- Vaccination remains mainstay of health maintenance in people with HIV, including introduction of new vaccines for common and emerging infections

Thank You!!

Questions?