Top 10 game changers in HIV clinical science

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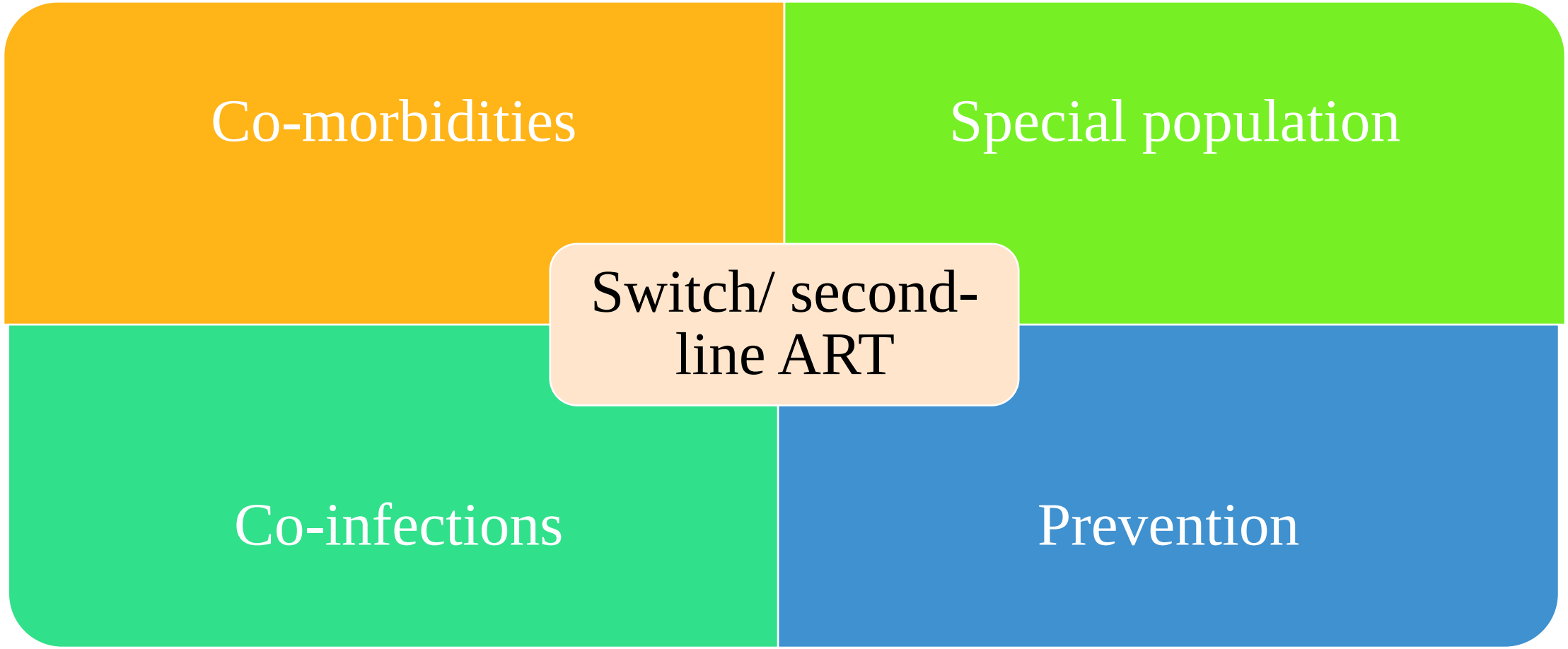
Selected areas



Switch/ second- line ART

	Long-acting therapy (n=255)	Oral therapy (n=257)	Difference (95% CI)*
Primary outcome			
HIV-1 viral load level			
<50 copies per mL	246 (96%)	250 (97%)	−0·8 (−3·7 to 2·3)
≥50 co			
No vir			
Primary			
HIV-1 vi			
<50 cc			
<50 cc			
<50 cc			
Seconda			
HIV-1 viral load <200 copies per mL	250 (98%)	252 (98%)	−0·01 (−2·4 to 2·4)
Confirmed virological failure‖	2 (1%)	0	0·8 (−0·7 to 2·8)
Confirmed virological failure (per protocol)‖	2 (1%)	0	..
Confirmed virological failure with ≥1 major acquired resistance mutation**	2 (1%)	0	..
Mean (SD) change from baseline in CD4 count, cells per mm³††	−13 (203)	13 (206)	−26 (−62 to 9)

Long-acting therapy had non-inferior efficacy compared with oral therapy, with a good safety profile, and can be considered for African treatment programmes.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Second-Line Switch to Dolutegravir for Treatment of HIV Infection

Table 2. Primary End Point at Week 48.

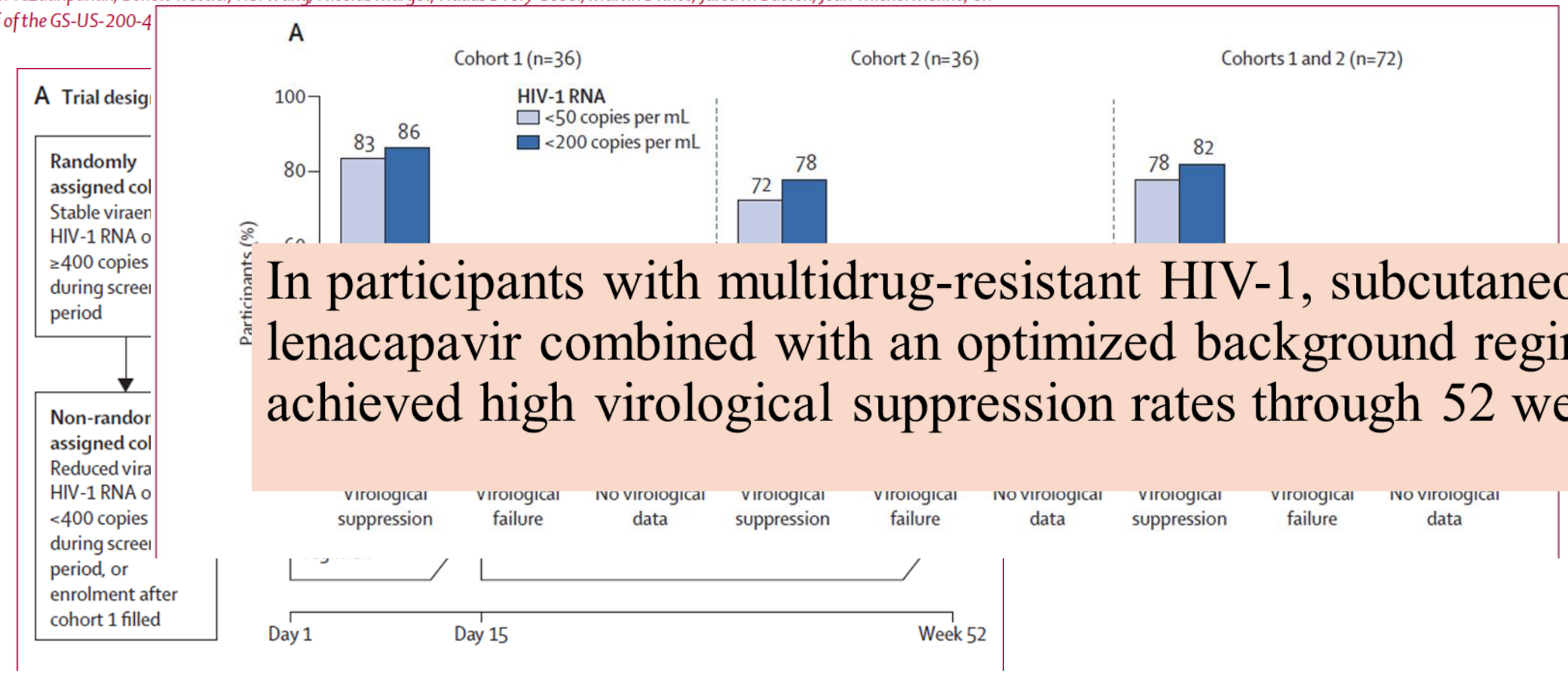
End Point	Dolutegravir (N=397)	Ritonavir-Boosted PI (N=394)	Difference (95% CI)*	P Value
	number (percent)		*percentage points*	
Primary end poin				
HIV-1 RNA ≥5				
Treatment dis efficacy				
Treatment dis with last a				
HIV-1 RNA <50 c				

In previously treated, virally suppressed patients without known drug resistance, switching to dolutegravir was noninferior to continuing a ritonavir-boosted PI regimen.

N Engl J Med 2023;388:2349-59.
DOI: 10.1056/NEJMoa2210005

Efficacy and safety of the novel capsid inhibitor lenacapavir to treat multidrug-resistant HIV: week 52 results of a phase 2/3 trial

Onyema Ogbuagu, Sorana Segal-Maurer, Winai Ratanasuwan, Anchalee Avihingsanon, Cynthia Brinson, Kimberly Workowski, Andrea Antinori, Yazdan Yazdanpanah, Benoit Trottier, Hui Wang, Nicolas Margot, Hadas Dvory-Sobol, Martin S Rhee, Jared M Baeten, Jean-Michel Molina, on behalf of the GS-US-200-4



In participants with multidrug-resistant HIV-1, subcutaneous lenacapavir combined with an optimized background regimen achieved high virological suppression rates through 52 weeks.

Lancet HIV 2023; 10: e497–505

Dolutegravir plus boosted darunavir versus recommended

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wi
no
fai

D²EFT

Stage 1 and

	Ritonavir-bo darunavir plu two NRTIs
HIV RNA at week 48	
Participants with data	
Missing data	
<50 copies per mL	
<200 copies per mL	
<400 copies per mL	
Baseline HIV RNA ≤10	
Participants with data	
Missing data	
<50 copies per mL	
<200 copies per mL	
<400 copies per mL	
Baseline HIV RNA >10	
Participants with data	
Missing data	1
<50 copies per mL	25 (57%)
<200 copies per mL	34 (77%)
<400 copies per mL	34 (77%)

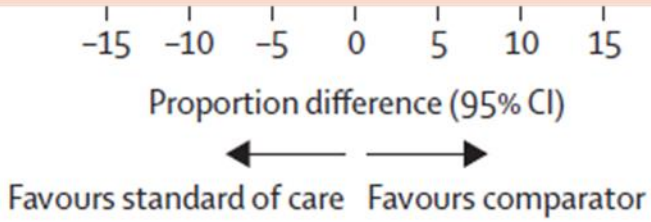
Efficacy percentages exclude participants
assigned but excluding administrative wit

Viral load at week 48

Standard of care group (ritonavir-boosted darunavir plus two NRTIs), n/N

Comparator group, n/N

Standard of care *vs* dolutegravir with tenofovir



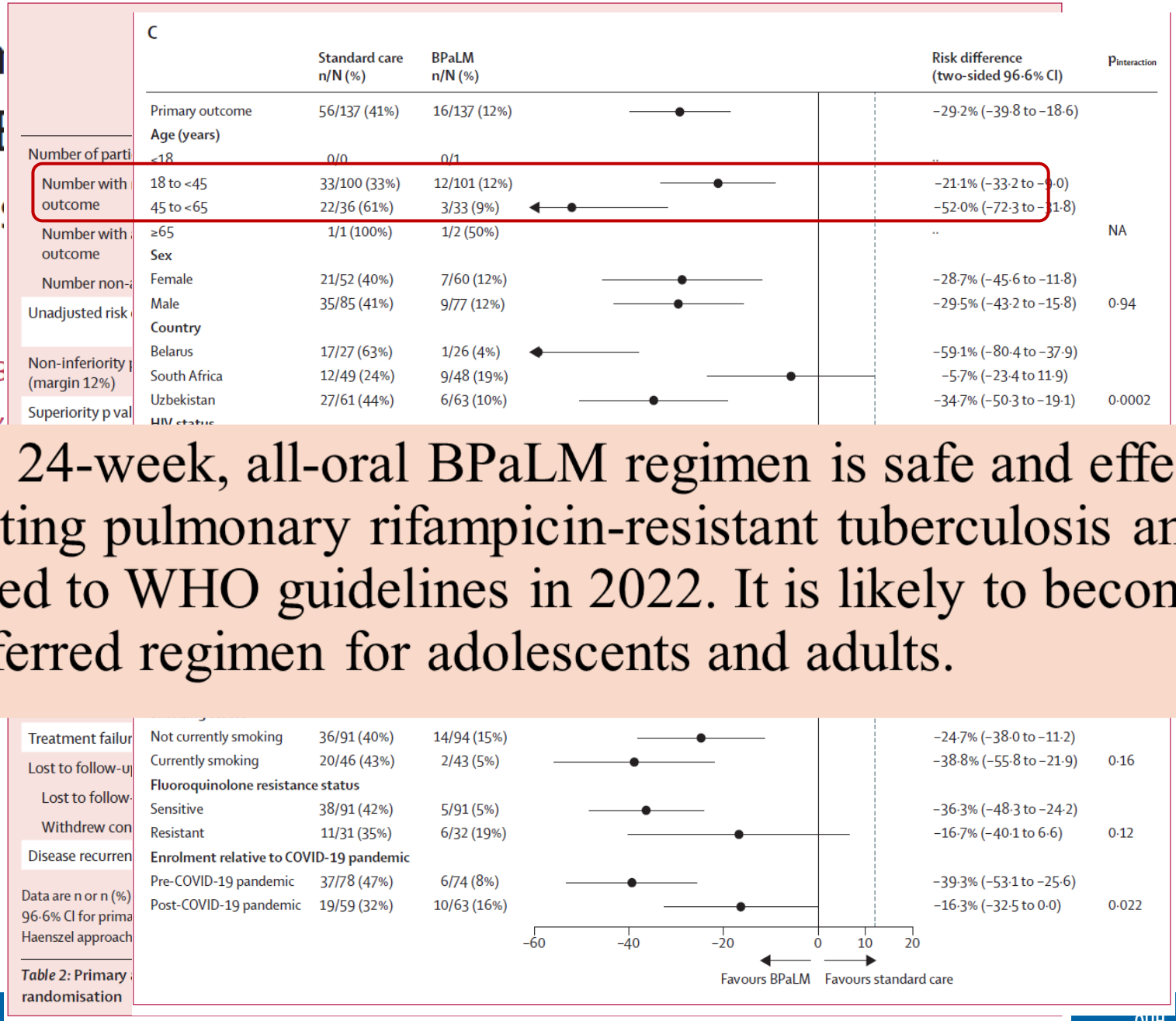
In individuals failing NNRTI-based first-line ART, switching to dolutegravir plus r/darunavir or dolutegravir with TDF and lamivudine/emtricitabine was non-inferior to r/darunavir with two NRTIs in achieving viral suppression, even without universal genotyping.

Lancet HIV 2024; 11: 436–48

Co-Infections: HIV/TB

Short oral regin
tuberculosis (TB
controlled, pha
non-inferiority

Bern-Thomas Nyang'wa, Catherine E
Varvara Solodovnikova, Irina Liverko,
Koert Ritmeijer, Philipp du C



The 24-week, all-oral BPaLM regimen is safe and effective for treating pulmonary rifampicin-resistant tuberculosis and was added to WHO guidelines in 2022. It is likely to become the preferred regimen for adolescents and adults.

Lancet Respir Med 2024; 12: 117–28

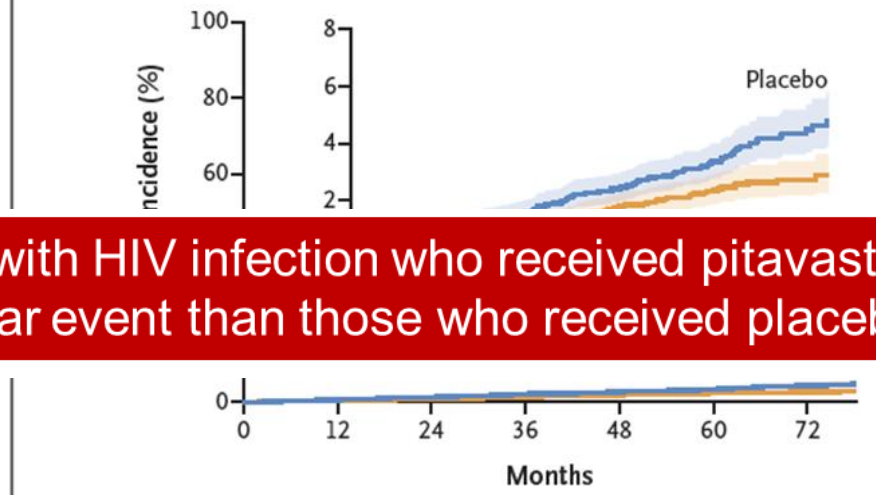
Co-morbidities

The NEW ENGLAND

A Estimated Treatment Effect

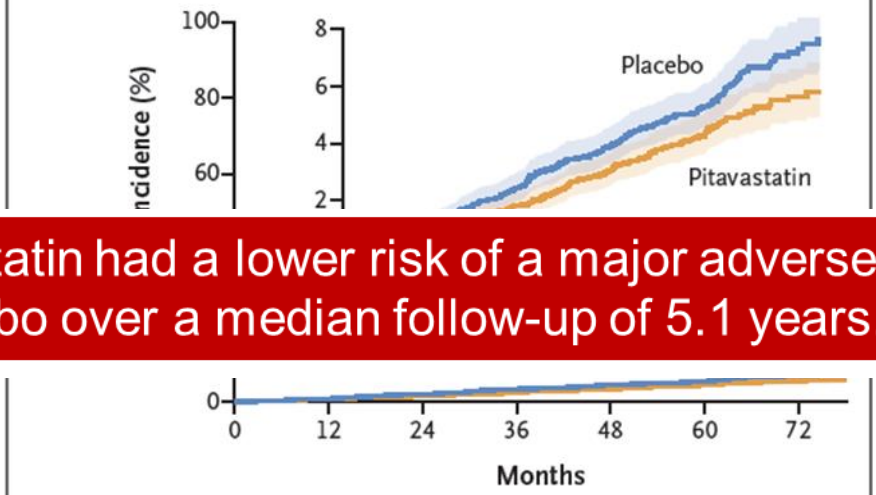
Subgroup	Pitavastatin (N=3888) no./1000 person-yr (no. of events)	Placebo (N=3881) no./1000 person-yr (no. of events)	Hazard Ratio (95% CI)
Primary outcome and supporting analyses			
First MACE	4.81 (89)	7.32 (136)	0.65 (0.48 to 0.90
First MACE including vital status follow-up	4.75 (90)	7.22 (137)	0.66 (0.50 to 0.86
First confirmed MACE	3.83 (71)	5.93 (110)	0.65 (0.48 to 0.87
First MACE (as-treated analysis)			
First MACE (per-protocol analysis)			
Secondary outcomes and supporting an			
First MACE or death			
First MACE or death including vital st			
Death from any cause			
Individual components of MACE			
First			
First			
First			
Dea			
Dea			
First cardiac catheterization or revasc			
First carotid or cerebrovascular revas			
First peripheral arterial revascularizat			

B First MACE



Cumulative Incidence of Event (%)							
Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73
No. at Risk							
Placebo	3881	3693	3506	3356	2997	2182	959
Pitavastatin	3888	3647	3475	3364	2997	1947	1052

C First MACE or Death



Cumulative Incidence of Event (%)							
Placebo	0.00	0.80	2.03	3.34	4.44	5.35	7.06
Pitavastatin	0.00	0.77	1.58	2.39	3.40	4.54	5.54
No. at Risk							
Placebo	3881	3693	3506	3356	2997	1975	919
Pitavastatin	3888	3647	3475	3364	2998	1948	1027

Participants with HIV infection who received pitavastatin had a lower risk of a major adverse cardiovascular event than those who received placebo over a median follow-up of 5.1 years.

The Effect of Open-Label Semaglutide on Metabolic Dysfunction–Associated Steatotic Liver Disease in People With HIV

- SLD is an independent CVD risk factor
- Semaglutide would reduce intrahepatic triglycerides

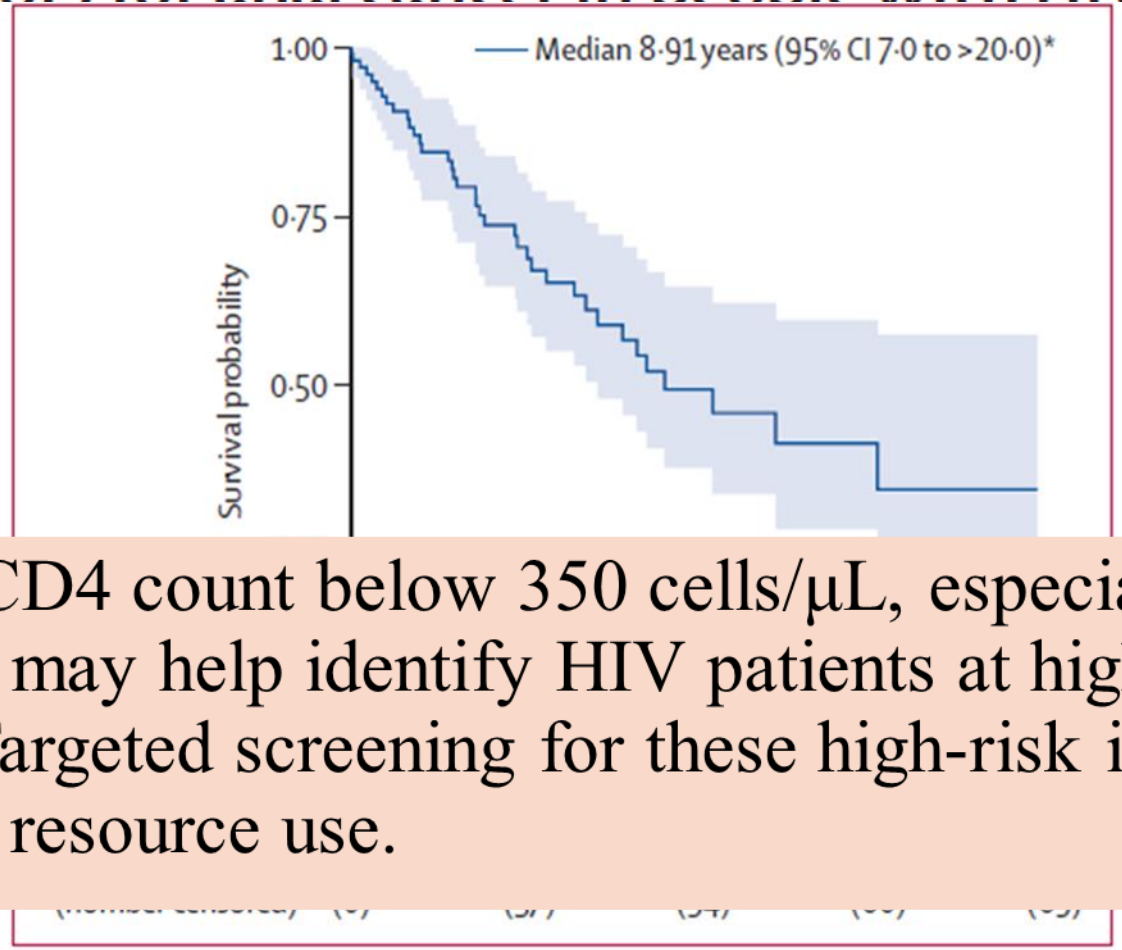
Table 2. Changes in IHTG, Cardiometabolic Parameters, and HIV-Associated Parameters

Outcome	Baseline	Week 24	Absolute Difference (95% CI)	Percentage Difference (95% CI)
Primary				
Mean IHTG (SD), *%**	12.7 (6.1)	8.5 (4.7)	−4.2 (−5.4 to −3.1)	−31.3 (−39 to −23.6)
Secondary				
Mean weight (SD), *kg*	103 (20.8)	95.1 (22.8)	−7.8 (−9.5 to −6.1)	−8.1 (−9.8 to −6.4)
Mean BMI (SD), *kg/m²*				
Mean waist circumference (SD), *c*				
Mean HOMA-IR score (SD)				
Mean fasting glucose level (SD), *r*				
Mean HbA_{1c} level (SD), *%*				
Mean fasting total cholesterol level (SD), *mg/dL*‡	175 (43.3)	174 (34.8)	−4.0 (−10.8 to 2.9)	−0.2 (−4.2 to 3.7)
Mean fasting triglyceride level (SD), *mg/dL*§	150 (87.9)	131 (75.8)	−26.8 (−46.0 to −7.5)	−10.5 (−20.8 to −0.2)
Mean fasting HDL cholesterol level (SD), *mg/dL*‡	46 (10.5)	47.6 (11.4)	2.0 (−0.02 to 4.1)	5.3 (0.6 to 10.0)
Mean fasting LDL cholesterol level (SD), *mg/dL*‡	101 (35.1)	102 (30.7)	−1.0 (−7.1 to 5.1)	3.0 (−4.5 to 10.4)
Other				
Mean ALT level (SD), *IU/L*	30.7 (13.4)	24.8 (11.9)	−6.1 (−9.5 to −2.6)	−15.3 (−23.8 to −6.7)
Elevated ALT level, *n (%)*‖	26 (53)	20 (41.7)	-	-
Mean $CD4^+$ T-lymphocyte count (SD), × *10^9 cells/L*	0.762 (0.340)	0.730 (0.302)	−0.014 (−0.081 to 0.053)	8.2 (−14.3 to 30.7)
HIV-1 RNA <50 copies/mL, *n (%)*	49 (100)	46 (97.9)	-	-

Semaglutide is an effective therapy for MASLD in PWH and shows evidence of broader cardiometabolic benefit

Identifying risk factors for anal cancer in people with HIV in Spain: a multicer … d in the PISCIS c…

Josep M Llibre, Boris Revoll…
Marta Navarro, Elena Leon…
Raquel Martin-Iguacel, on b…



A nadir CD4 count below 350 cells/µL, especially under 200 cells/µL, may help identify HIV patients at higher risk for anal cancer. Targeted screening for these high-risk individuals could optimize resource use.

Figure 3: **Survival analysis in people with HIV diagnosed with anal cancer**
*The upper limit extends beyond 20 years because it is constrained by the study's 20-year period and the insufficient number of events in this period.

Figure 1: Incidence rate…
Point estimates are shov…
30–44 years, 45–59 years, …

Lancet HIV 2024

Special population

Long-Acting Injectable CAB/RPV is Superior to Oral ART in PWH With Adherence Challenges: ACTG A5359 – CROI 2024

Phase III, randomized, open-

- PWH with persistent HIV-1 RNA >200
- Endpoin
  failure (
  confirm
  RNA>2
  treatmen
  discontinuation

Table: Kaplan-Meier cumulative probabilities for primary and key secondary endpoints and difference in probabilities between LAI and SOC arms

Endpoint	CAB-LA/RPV-LA (n= 145*)		SOC (n=148)		Difference (nominal 98.75% CI)
	Failure, n	Cumulative Probability	Failure, n	Cumulative Probability	
Primary: Regimen failure (virologic	28 (5+23)#	24.1%	47 (28+19)	38.5%	-14.4% (-29.8%, 0.8%)
discontinuation					

* One participant with ART information pending was excluded from the interim efficacy analyses. # One participant assigned to LAI had treatment discontinuation as the primary endpoint but subsequently experienced VF.

LA Cabotegravir & rilpivirine injections, administered monthly or every other month, offer an effective HIV treatment option for individuals struggling with daily pill adherence and maintaining viral suppression.

Feb 12, 2024, DSMB halted the study due to superior efficacy of LA CAB+RPV in secondary endpoints

Prevention

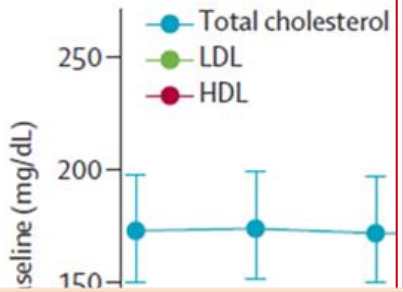
HIV-1 infection kinetics, drug resistance, and long-term safety of pre-exposure prophylax tenofovir alafena

	Proteinuria
	Total†
Baseline	25/2687 (0·9
Week 48	25/2361 (1·1
Week 96	27/2181
Week 144	15/1919

Data are n/N (%) or median per
22·6 mg/mmol. UPCR=urine pr
received emtricitabine and tenc
at each timepoint (including th
the number of participants witl
timepoint and N is the number

Table 1: Quantitative proteinuri
144 weeks of emtricitabine and

F Fasting lipids and gluc



Time since bas

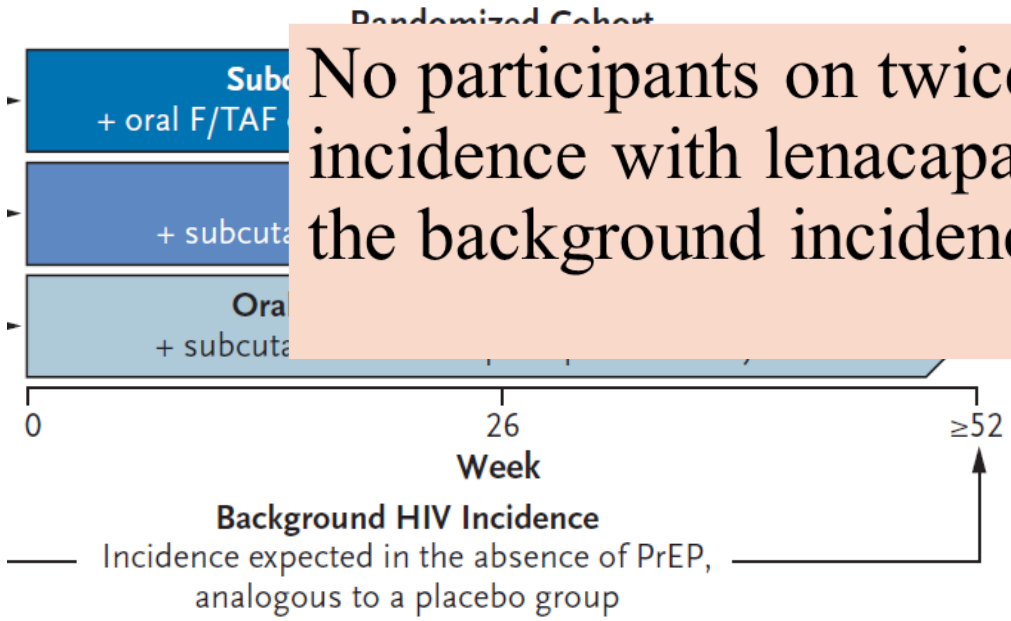
Number assessable (lipids)	1412	1160	1148
Number assessable (glucose)	1426	1332	1216

	Total population
Any treatment-emergent adverse event	2544 (94%)
Any grade 3 or 4 treatment-emergent adverse event	67 (3%)
Discontinuation of study drug due to adverse event	43 (2%)
Serious adverse events*	257 (10%)
Serious adverse events related to study drug†	3 (<1%)
Deaths‡	7 (<1%)
Nasopharyngitis	468 (17%)
Upper respiratory tract infection	456 (17%)
Urethritis chlamydial	394 (15%)
Urethritis gonococcal	295 (11%)

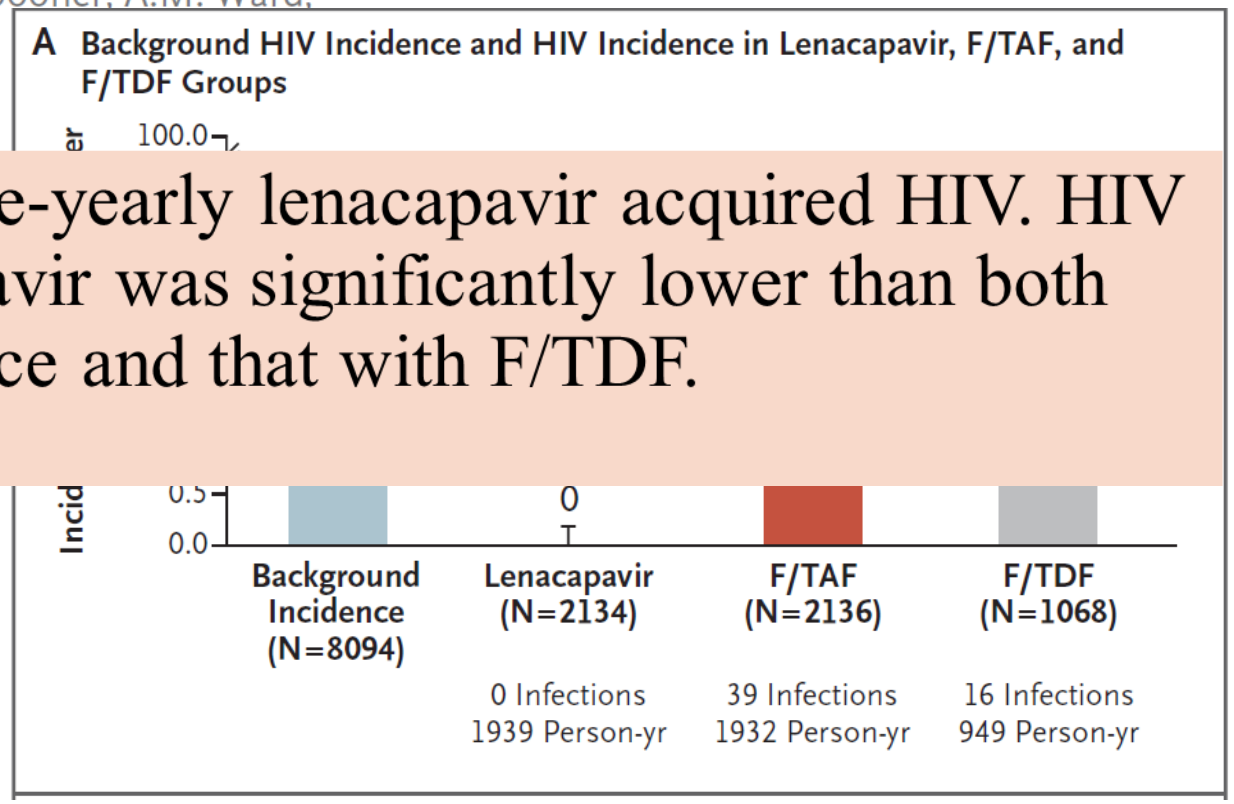
Routine HIV-1 RNA testing for individuals on daily oral PrEP offers modest clinical benefit. Long-term use of emtricitabine and tenofovir alafenamide as daily PrEP is safe, well tolerated, and suitable for those with bone or renal conditions.

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batting, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. and F. Matovu Kiweewa, for the PURPOSE 1 Stu



No participants on twice-yearly lenacapavir acquired HIV. HIV incidence with lenacapavir was significantly lower than both the background incidence and that with F/TDF.



Wrap-up

- Long-acting injectable regimens show promise as second-line therapy, particularly in MDR-HIV.
- Dolutegravir-based regimens are robust for treatment-experienced patients and those failing NNRTI-based ART.
- BPaLM regimen is a new standard for rifampicin-resistant TB treatment.
- Statins and semaglutid are effective in reducing CVD risk
- Nadir CD4 counts can be useful in identifying HIV patients at higher risk of anal cancer, allowing for targeted screening.
- Long-term PrEP is safe, particularly for those with bone or renal concerns and new PrEP regimens are in development