EACS 2023: Highlights from the European AIDS Conference in Warsaw

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This activity is jointly provided by Physicians' Research Network and the Medical Society of the State of New York.

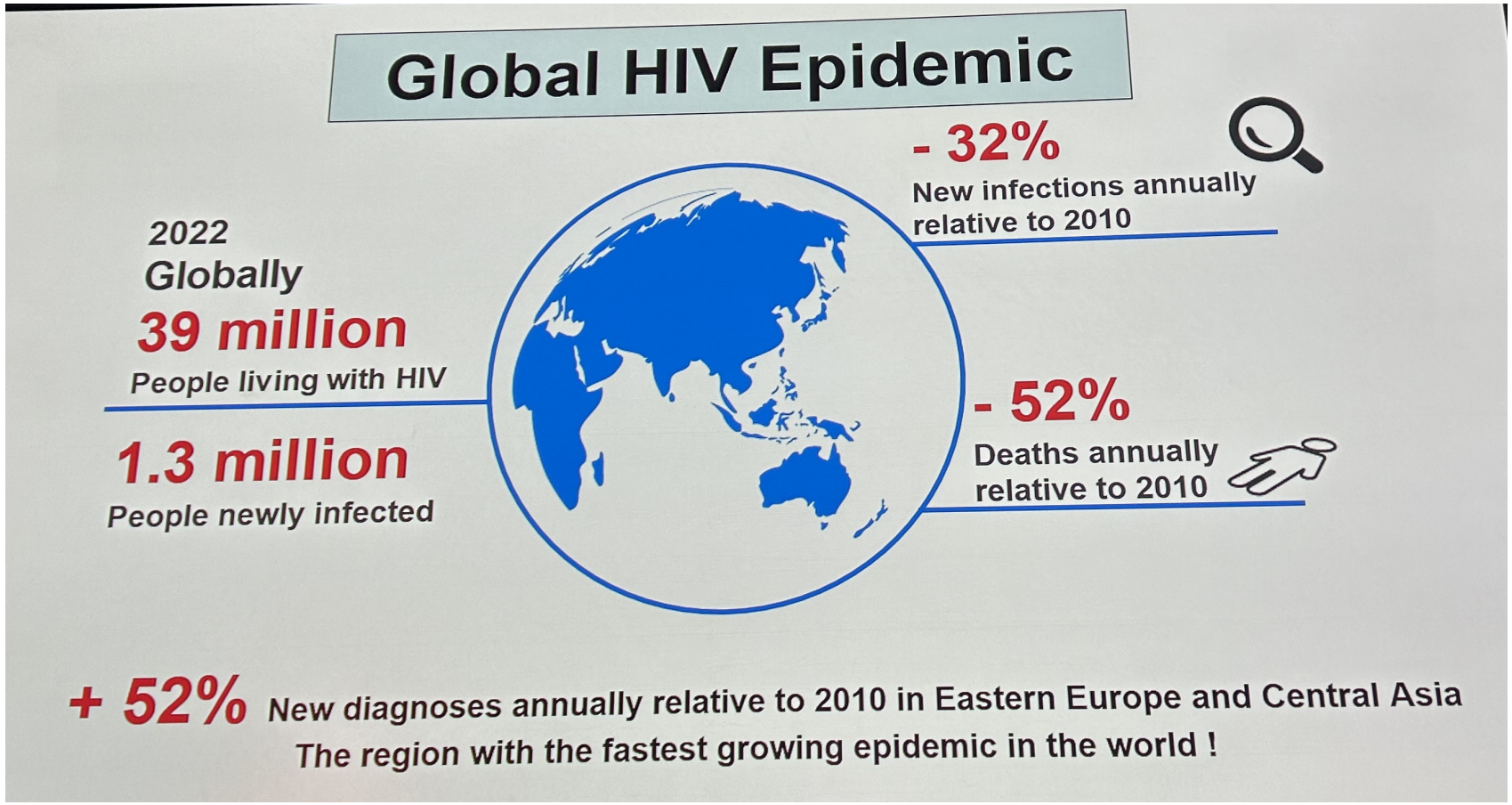
Conflict of Interest: JKR

- **Honoraria for lectures and/or consultancies from Abbvie, Berlin Cures, Boehringer, Galapagos, Gilead, Janssen, MSD, and ViiV.**

- **Research grants from Dt. Leberstiftung, DFG, DZIF, Hectorstiftung, NEAT ID.**

EACS Conference 2023

» HIV Epidemiology in Europe



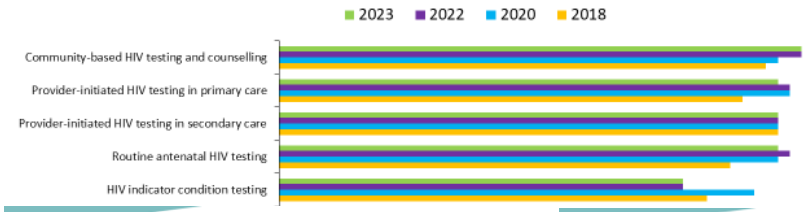
UNAIDS/WHO estimates presented by JM Molina at EACS 2023

Inequities in prevention, testing and clinical outcomes

~107,000 persons were diagnose
WHO European Region in 2

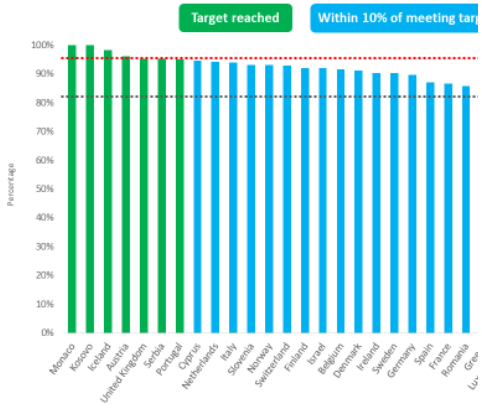
Number of people receiving PrEP in the last 12 months, 2022

Countries implementing different testing services over time, 2018-2023

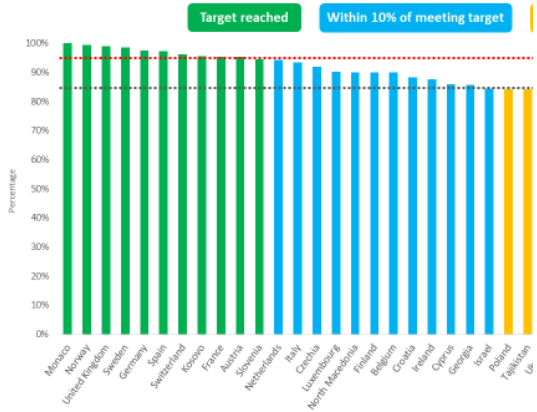


plementation in Europe

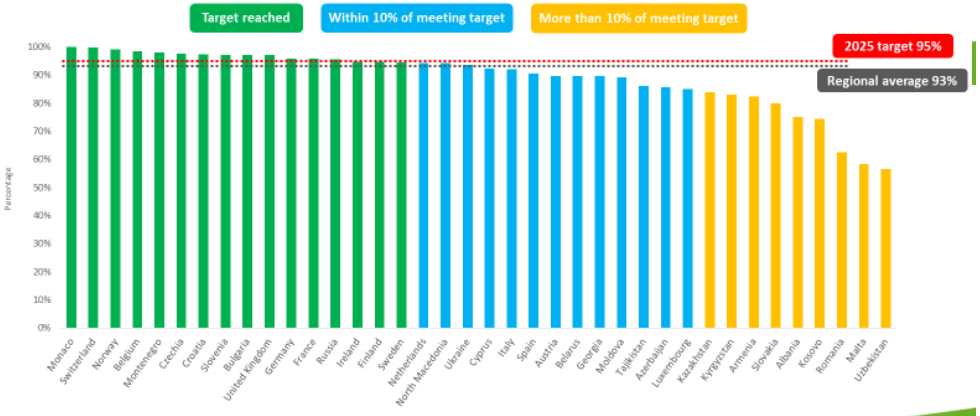
Progress toward the 1st 95%
95% of all PLHIV who know their stat



Progress toward the 2nd 95% ta
95% of those diagnosed on ART (n=43 c



Progress toward achieving the 3rd 95:
90% of those on ART virally suppressed (n=38 countries)



Source: ECDC. Continuum of HIV care. Stockholm: ECDC; 2025. In Press.

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Need for European standards of HIV care

- Scoping project and expert meeting at EACS Basel (2019)
- Development of a European Standard of Care for PLHIV covering the European region would be of added value
- The SoC should be kept short and proceed in a step-wise manner
- The SoC should include auditable and measurable indicators
- Regular audits to measure SoC implementation should be kept short and focus on a few selected topics
- **COVID-19 halted progress**

ECDC tender on European standards of HIV care, 2022

Objectives:

1. To define sta
along the ca
and related
measurable
outcomes

2. To develop
used to au
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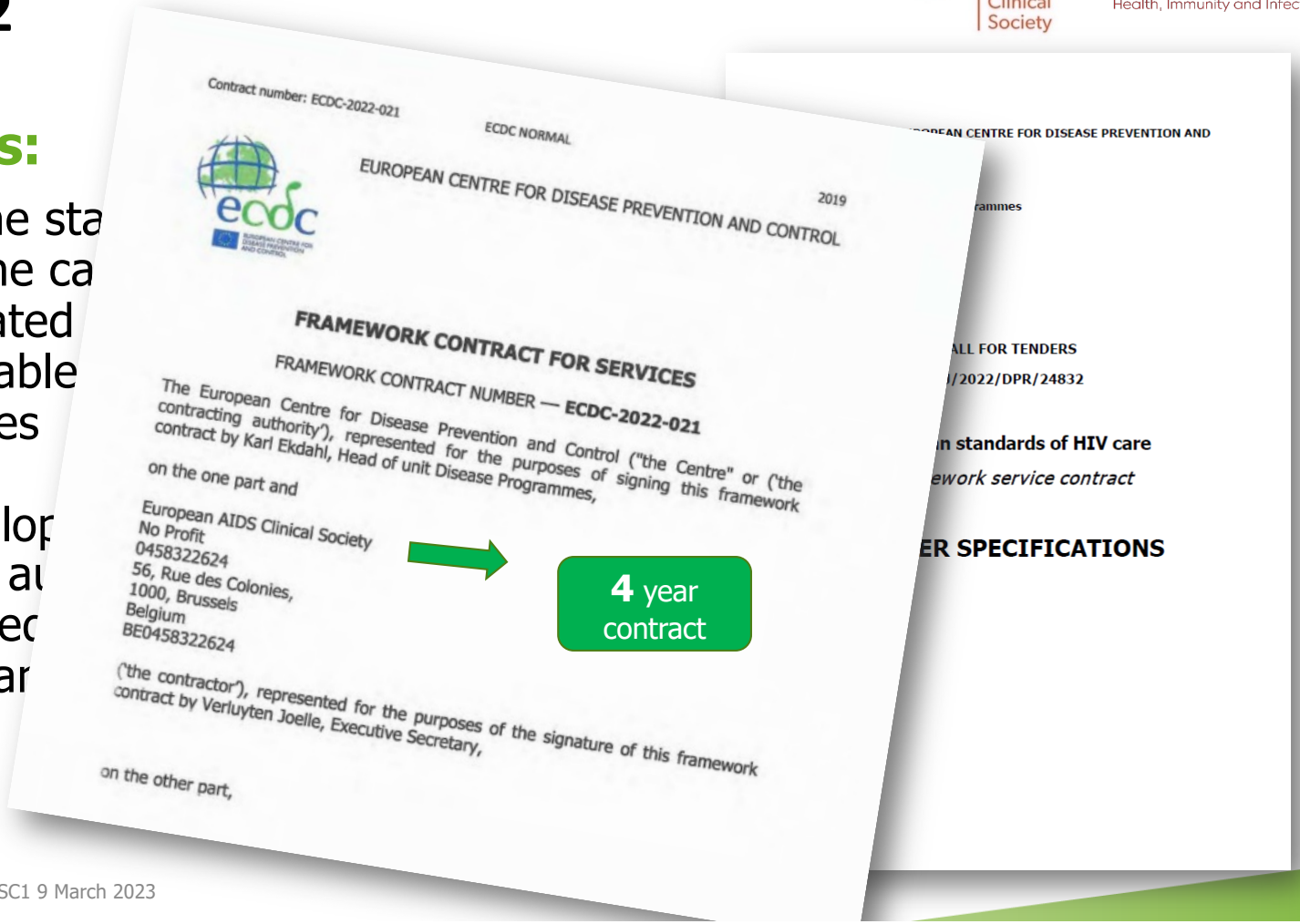
clinical ar



Key elements of the project

Standard of care modules

Audits

Scientific manuscripts

Support implementation of standards
(country support tender)

ECDC advisory group meetings

Annual workshops at EACS conferences

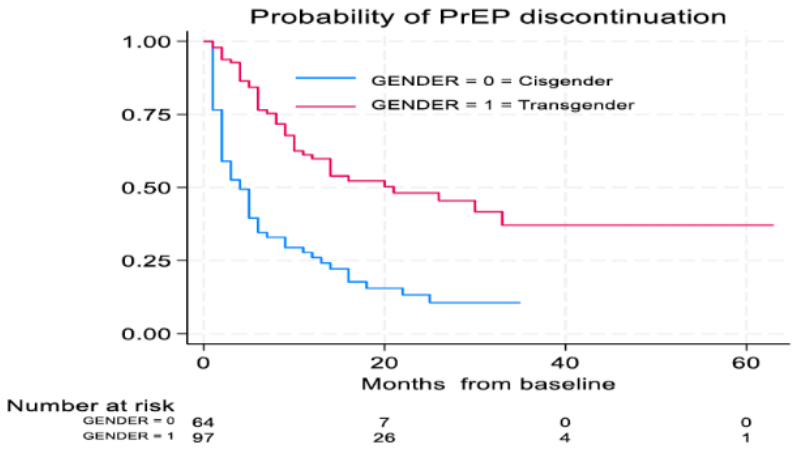
Assess implementation of standards
(Dublin monitoring)

» **Anything new in prevention?**

Factors influencing discontinuation of care of women seeking Pre-Exposure Prophylaxis (PrEP)

Objective: To describe which women are seeking PrEP (n=175) in a tertiary sexual health center in France and estimate risk factors associated with retention in care.

Predicted probability of prEP discontinuation over time by gender



Factors associated with PrEP discontinuation

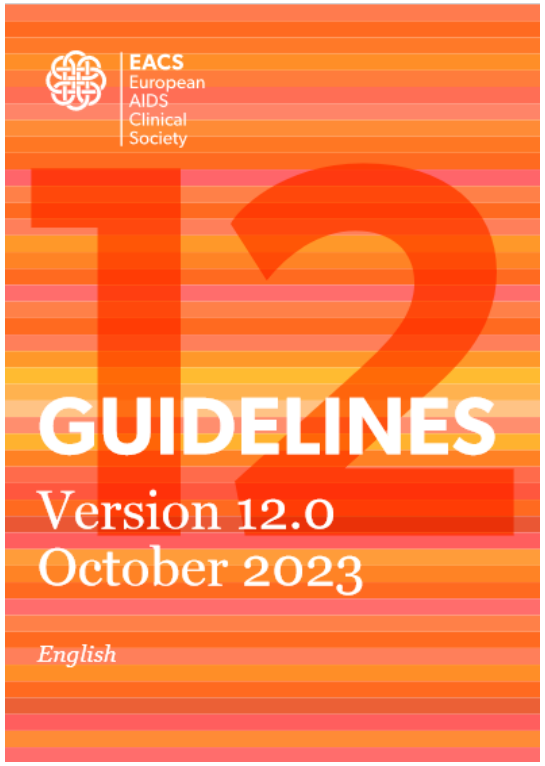
	Cox unavailable regression[1]		*Cox multivariable regression*[3]	
	Non-adjusted HR of PrEP discontinuation (95% CI)	**p-value**[2]	**Adjusted HR of PrEP discontinuation (95% CI)**	**p-value**
Gender identity				
Cisgender women		*Reference*		
Transgender women	0.32 (0.22 - 0.48)	**<0,01**	0. 36 (0.23– 0.56)	**<0,01**
STI in the last 12 months before PrEP				
No		*Reference*		
Yes	0.53 (0.36 – 0.79)	**0.002**	0.78 (0.51 – 1.21)	0.219
Chem-sex[4]				
No		*Reference*		
Yes	0.52 (0.33 – 0.84)	**0.007**	N/A	N/A
Unprotected sex				
No		*Reference*		
Yes	0.53 (0.33 – 0.85)	**0.009**	0.91 (0. 54 – 1.52)	0.452
Origin				
South America		*Reference*		
Europe	1.31 (0.78 - 2.19)	0.312	1.35 (0.79 - 2.31)	0.268
Africa	2.50 (1.14 - 5.47)	**0.022**	2.54 (1.14 - 5.67)	**0.023**

[1]Factors associated with PrEP discontinuation were analyzed using Kaplan-Meier curves and Cox univariable regression.
[2]In univariable analysis, transgender identity, STI in the last 12 months before PrEP*, unprotected sex, chem-sex and* African *origin were significantly associated with discontinuation/retention in PrEP care.*
[3]All variables with p<0.05, except "Chem-sex" were further analyzed in a Cox proportional hazards multivariable regression model.
[4]The proportional-hazards assumption based on Schoenfeld residuals was violated for "Chem-sex" – this variable was included in the model as a stratification variable.

Melnyk T et al. EACS 2023

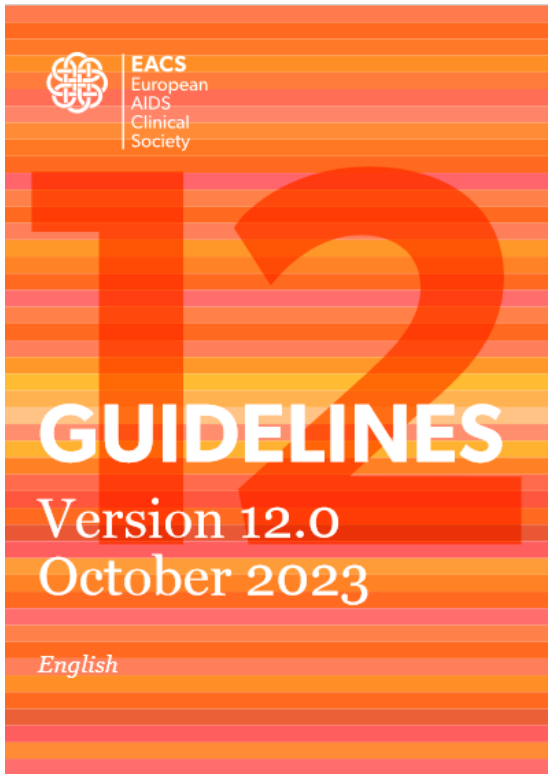
And what do the guidelines say?

- Counsel that PrEP does not prevent other types of STIs; screen for STI (syphilis, chlamydia, gonorrhoeae, HAV, HCV) when starting PrEP and regularly during use of PrEP, pages 7-9
  All persons under PrEP should be offered vaccinations against HAV, HBV, HPV and monkeypox virus.
  Doxycycline post exposure prophylaxis, 200 mg within 24 to 72h after sexual intercourse, proved to be effective in preventing bacterial STIs in MSM with the caveat of the unknown long terms effects on microbiota and STIs resistance. It can be proposed to persons with repeated STIs on a case by case basis.



» New Data on ART

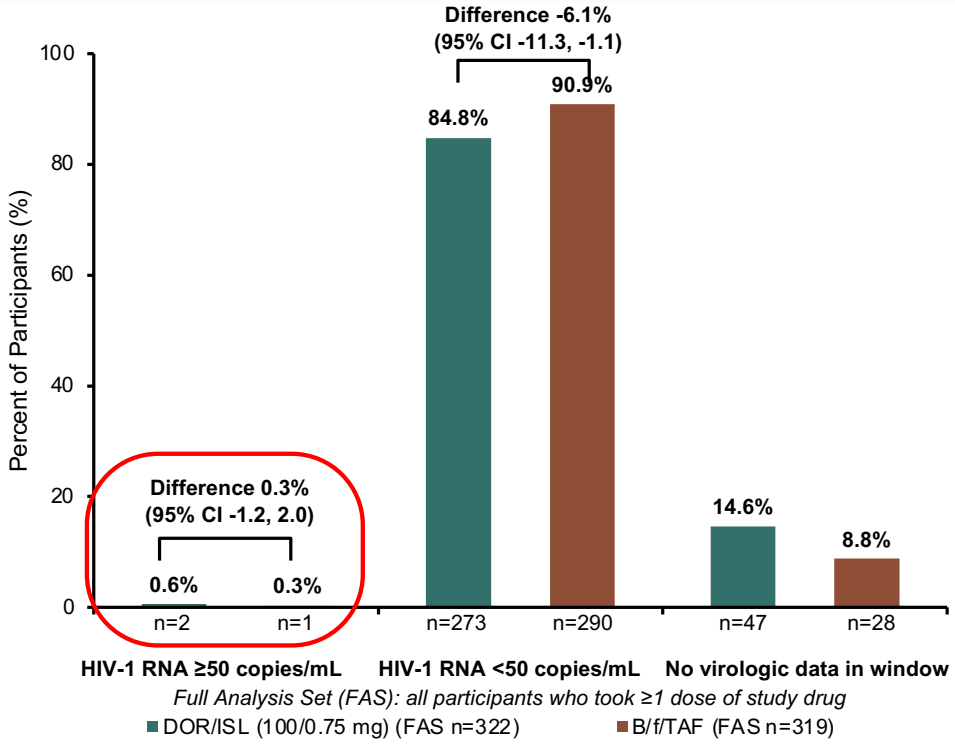
EACS Guidelines version 12.0



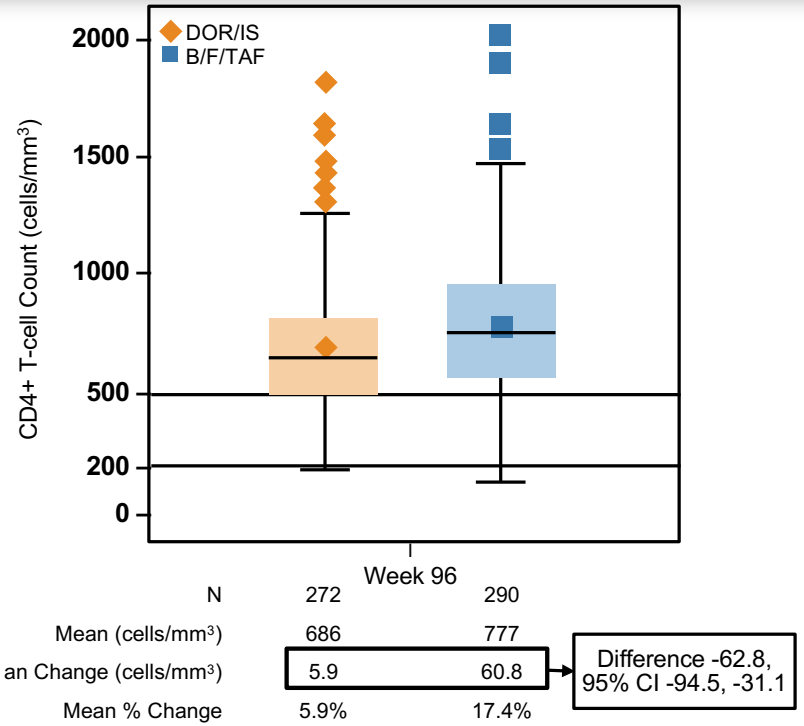
ART is recommended in all adult persons with HIV, irrespective of CD4 counts[i]

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk) II (Weight increase (DTG))
TAF/FTC/BIC		II (Weight increase (BIC, TAF))
TAF/FTC or TDF/XTC + DTG		II (Weight increase (DTG, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing)
TAF/FTC or TDF/XTC + RAL qd or bid		II (Weight increase (RAL, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	II (Weight increase (DTG)) V (3TC/DTG not after PrEP failure)
2 NRTIs + NNRTI		
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR		II (Weight increase (TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (DOR: caveats, HIV-2)
Alternative regimens		
2 NRTIs + NNRTI		
TAF/FTC or TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner	II (Weight increase (TAF) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VII (EFV: neuro-psychiatric adverse events. HIV-2 or HIV-1 group 0, dosing)
TAF/FTC or TDF/XTC + RPV or TAF/FTC/RPV or TDF/FTC/RPV	CD4 count > 200 cells/µL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food	II (Weight increase (TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VIII (RPV: HIV-2)
2 NRTIs + PI/r or PI/c		
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food	II (Weight increase (TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IX (DRV/r: cardiovascular risk) X (Boosted regimens and drug-drug interactions)

Switch to F Doravirine/Islatravir (100/0.75 MG) vs Maintenance Of Bictegravir/Emtricitabine/Tenofovir Alafenamide: Week 96 Results



DOR/ISL comparable to B/F/TAF for HIV-1 RNA <50 copies/mL in mFAS

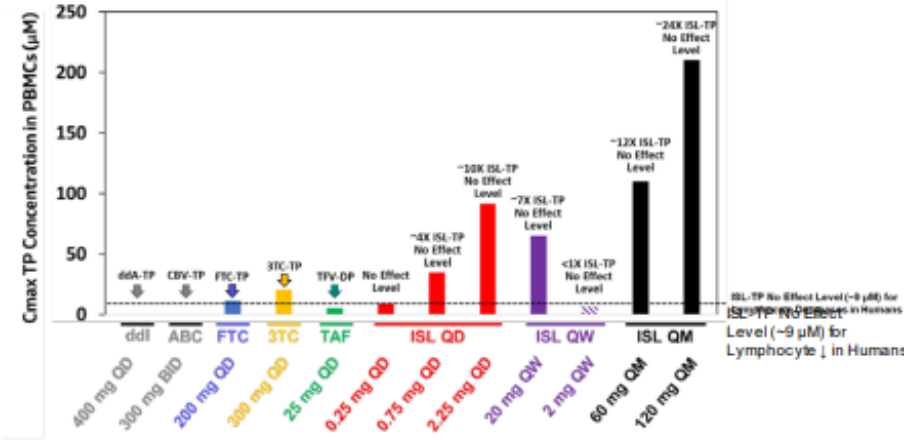


- 2 participants with confirmed viremia in DOR/ISL group likely due to non-adherence
- No DOR or ISL resistance was observed through Week 96

Paredes R, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS1.O1.

Studies to understand the decease in Lymphocytes

ISL-TP Cmax Levels in Human PBMCs Associated with ↓ Lymphocytes Were 4- to 24-times Higher Than Those Observed at the ISL Dose That Did Not Cause ↓ in Lymphocytes (0.25 mg QD), & Were Also Higher Than TP Levels Achieved by Approved NRTIs



- These data, together with clinical & modeling data, identified an ISL-TP threshold (9 μM), and subsequently ISL QD and QW clinical doses below which decreases in lymphocytes are not expected

Lebron JA et al. EACS 2023

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Weak Human Polymerase α Inhibition at High TP Levels is Common to Most NRTIs and is a Plausible Mechanism for Lymphocyte Decreases

Compound	Polymerase α IC_{50} or Ki (μM)
ISL-TP	30
TFV-DP (TP of TAF)	5
FTC-TP	6
Carbovir-TP (TP of Abacavir)	22
3TC-TP	175
ddA-TP (TP of ddI)	>500

- Like NRTIs, ISL inhibits DNA polymerase α (IC_{50} = 30 μM)
- ISL did not inhibit DNA polymerase β or mitochondrial DNA polymerase γ at up to 200 μM (highest concentration tested)

If NRTIs inhibit polymerase α, why then did they not cause lymphocyte decreases clinically?

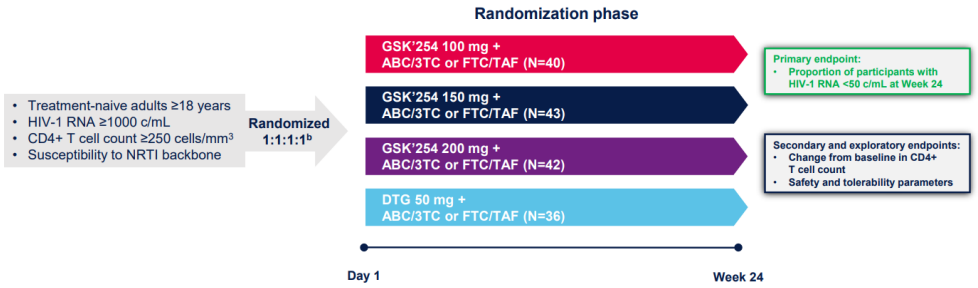
Conclusions

- Accumulation of high ISL-TP concentrations in lymphocytes can lead to cytotoxicity, possibly through DNA polymerase α inhibition as a contributing factor.
- These effects are shared with several marketed NRTIs, at similarly high triphosphate levels.
- Mitochondrial toxicity is not a contributing mechanism.
- These investigations, together with clinical and modelling data, identified an ISL-TP threshold (9 μM), and subsequently ISL QD and QW clinical doses below which decreases in lymphocytes are not expected.

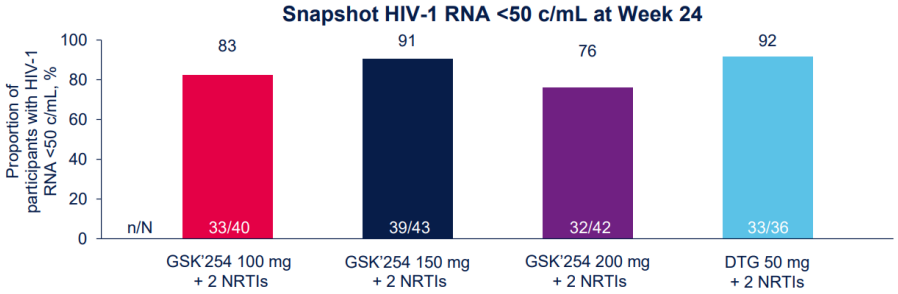
New maturation inhibitor

Study Design and Endpoints

- DOMINO was a partially blinded, active-controlled, phase 2b trial in which treatment-naive participants were randomized to receive once-daily oral GSK'254 100, 150, or 200 mg (blinded dose) with a low-fat meal[a] or open-label DTG, all with 2 open-label NRTIs



Results: Week 24 Efficacy



- GSK'254 + 2 NRTIs demonstrated generally high and comparable efficacy to DTG + 2 NRTIs
- Mean increases from baseline to Week 24 in CD4+ T cell count were observed across the GSK'254 + 2 NRTIs groups (129.3 to 241.3 cells/mm^3) and the DTG + 2 NRTIs group (198.5 cells/mm^3)

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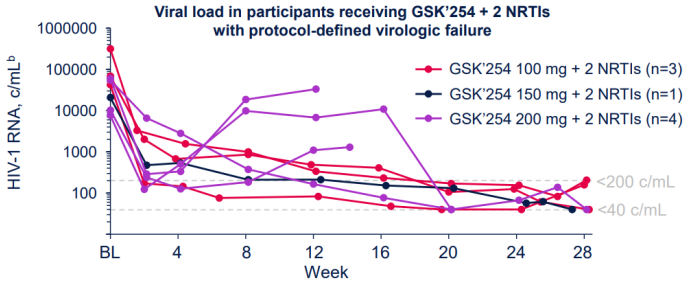
Protocol defined virological failure

- Protocol-defined virologic failure[a] occurred in 8 participants receiving GSK'254 + 2 NRTIs (100 mg, n=3 [8%]; 150 mg, n=1 [2%]; 200 mg, n=4 [10%]) and 1 (3%) receiving DTG + 2 NRTIs
  - 7 of 9 participants with protocol-defined virologic failure met criteria at or before the Week 24 visit
- 4 of 9 participants with protocol-defined virologic failure had HIV-1 RNA <200 c/mL



- No treatment-emergent resistance was detected at protocol-defined virologic failure or before Week 24 across all groups[c]

[a]Protocol-defined virologic failure criteria included: decrease from baseline of HIV-1 RNA <1.0 $\log_{10}$ by Week 12; confirmed HIV-1 RNA ≥200 c/mL at or after Week 24; HIV-1 RNA ≥50 c/mL on repeat testing at Week 24 and before Week 28; confirmed HIV-1 RNA ≥200 c/mL after confirmed consecutive plasma HIV-1 RNA <50 c/mL. [b]All plot points at 40 c/mL indicate a value of <40 c/mL. [c]4 of 5 participants had results from resistance tests; the assays failed for 1 participant.

- The maturation inhibitor GSK'254 demonstrated generally comparable efficacy and safety/tolerability to DTG on a backbone of 2 NRTIs without treatment-emergent resistance
- Ultimately, ViiV Healthcare determined that the intended phase 3 fixed-dose combination of GSK'254-containing daily oral regimen would not be differentiated enough from existing 2-drug daily oral regimens; thus, GSK'254 was not advanced into phase 3
- However, the DOMINO data support further investigation of the next maturation inhibitor, GSK3739937, which has potential to be used as a partner agent in a long-acting regimen[1] and has recently started a phase 2a proof-of-concept study (NCT06061081)

1. Benn et al. *Pharmacol Res Perspect*. 2023;11:e01093.

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VICDOR Study

Table 1: Baseline characteristics of individuals who switched to DOR-based ART between JAN 2019 and SEP 2021 in Germany

Age [years]	**Median (range)**
Age at the time of switch	49 (21 – 78)
Gender at birth	n (%)
Male	164 (85.0)
Female	29 (15.0)
Body weight [kg]	**Median (range)**
Body weight at the time of switch	85.0 (42.9 – 137.0)
BMI [kg/m²] (categorical)	**n (%)**
Underweight (BMI <18.5)	2 (1.0)
Normal weight (BMI ≥18.5 to <25)	57 (29.5)
Overweight (BMI ≥25 to <30)	69 (35.8)
Obese Class 1 (BMI ≥30 to <35)	35 (18.1)
Obese Class 2 (BMI ≥35 to <40)	7 (3.6)
Obese Class 3 (BMI ≥40)	4 (2.1)
Missing	19 (9.8)
Time since HIV-1 diagnosis [years]	**Median (range)**
Time since HIV-1 diagnosis at the time of switch	11 (1 – 35)
Comorbidities	**n (%)**
Yes	156 (80.8)
No	37 (19.2)
Most frequent comorbidities	**n (%)**
Arterial hypertension	59 (30.6)
Psychiatric disorder	43 (22.3)
Disorder of lipid metabolism	35 (18.1)
Bone and bone metabolism disorder	30 (15.5)
Cardiac, cardiovascular, or cerebrovascular disorder	28 (14.5)
Comedication with statins	**n (%)**
Yes	33 (17.1)
No	160 (82.9)

3TC, lamivudine; ART, antiretroviral therapy; BMI, body mass index; CNS, central nervous system; DOR, dorevirine; DTG, dolutegravir; INSTI, integrase strand transfer inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitors; PWH, People with HIV-1; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

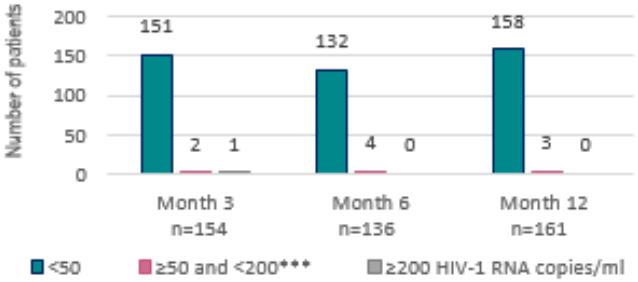
Table 2: Prior ART and DOR-based regimen of individuals who switched to DOR-based ART between JAN 2019 and SEP 2021 in Germany

Anchor class of most recent ART prior to switch	**n (%)**
INSTI	121 (62.7)
DTG-containing	52 (26.9)
BIC-containing	46 (23.8)
NNRTI	48 (24.9)
PI	21 (10.9)
Other	2 (1.0)
Missing[1]	1 (0.5)
TAF contained in most recent ART prior to switch	**n (%)**
Yes	113 (58.5)
No	80 (41.5)
Number of total previous ART regimens	**Median (range)**
Number of previous ART regimens since HIV-1 diagnosis before switch	3 (1 – 15)
Reason for switch to DOR-based ART (multiple answers possible)	**n (%)**
Tolerability regarding weight gain	72 (37.3)
Tolerability regarding other aspects	35 (18.1)
Treatment simplification and convenience	19 (9.8)
Tolerability regarding CNS symptoms	16 (8.3)
Reduce potential for drug-drug interactions	15 (7.8)
Improve management of comorbidities	9 (4.7)
Better immunologic control	1 (0.5)
Economic motivation	1 (0.5)
Other reason[2]	21 (10.9)
Reason cannot be determined	12 (6.2)
DOR-based ART regimens	**n (%)**
DOR/3TC/TDF	163 (84.5)
DOR/DTG	20 (10.4)
Other[3]	10 (5.2)

[1]In case of missing information regarding the most recent ART, the use of a DOR-based regimen was excluded via verification of the inclusion criteria.
[2]This could include any reason not listed above.
[3]These included DOR/3TC/DTG, DOR/TAF/FTC, DOR/3TC/ABC, DOR/DTG/ABC, DOR/DTG/FTC, DOR/DTG/TAF, DOR/RAL and DOR/TDF/DTG.

Figure 2: Virologic suppression* and virologic failure**

Patients who have continued DOR treatment and had a viral load measurement (HIV-1 RNA copies/ml blood) at the respective timepoint



*** Per protocol, these patients needed to have a follow-up visit with a viral load <50 copies/ml to be regarded as virologically suppressed.

Of the three patients with viral loads of ≥50 to <200 copies/ml at month 12, two

Wyen C et al. HIV Drug Therapy, EACS 2023

VICDOR Study

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Table 3: CD4+ T-cells – Change from baseline

Time after switch	Number of patients (n)	Median (IQR) (cells/µl)
Month 3	148	+2.0 (-79.5 – 102.5)
Month 6	131	+5.0 (-76.0 – 101.0)
Month 12	154	+13.0 (-97.0 – 118.0)

Only patients who stayed on their baseline DOR-regimen and with available data at baseline and the respective timepoint were included in the analysis.

Table 4: LDL-C – Change from baseline

Patients with available data at baseline, month 6 and month 12

	Total		Patients who switched to DOR/3TC/TDF (subgroup analysis)	
Time after switch	Number of patients (n)	Median (IQR) (mg/dl)	Number of patients (n)	Median (IQR) (mg/dl)
Month 6	89	-10.0 (-25.0 – 5.0)	80	-12.0 (-26.0 – 4.0)
Month 12	89	-7.1 (-23.0 – 8.0)	80	-10.5 (-23.5 – 8.0)

Only patients who stayed on their baseline DOR-regimen and with available data at baseline, month 6 and month 12 were included in the analysis.

Table 5: Weight – Change from baseline

Patients with available data at baseline, month 6 and month 12 who switched to DOR/3TC/TDF

	Total		Patients who switched to improve tolerability regarding weight gain (subgroup analysis)		Patients who switched from TAF-containing regimens (subgroup analysis)		Patients who switched from INSTI-based regimens (subgroup analysis)	
Time after switch	Number of patients (n)	Median (IQR) (kg)	Number of patients (n)	Median (IQR) (kg)	Number of patients (n)	Median (IQR) (kg)	Number of patients (n)	Median (IQR) (kg)
Month 6	50	-0.6 (-2.6 – 1.0)	23	-1.0 (-3.0 – 1.0)	30	-1.1 (-3.5 – 1.0)	31	0.0 (-1.5 – 1.4)
Month 12	50	-0.9 (-4.0 – 2.0)	23	-2.0 (-5.0 – -1.0)	30	-1.0 (-4.9 – 2.0)	31	-1.0 (-2.8 – 3.0)

Only patients who stayed on their baseline DOR-regimen and with available data at baseline, month 6 and month 12 were included in the analysis.

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Virologic Outcomes of Lamivudine/Dolutegravir in Virologically Suppressed Persons With Expected or Confirmed Resistance to Lamivudine (VOLVER Clinical Trial)

» **Key inclusion criteria**

Virologically suppressed

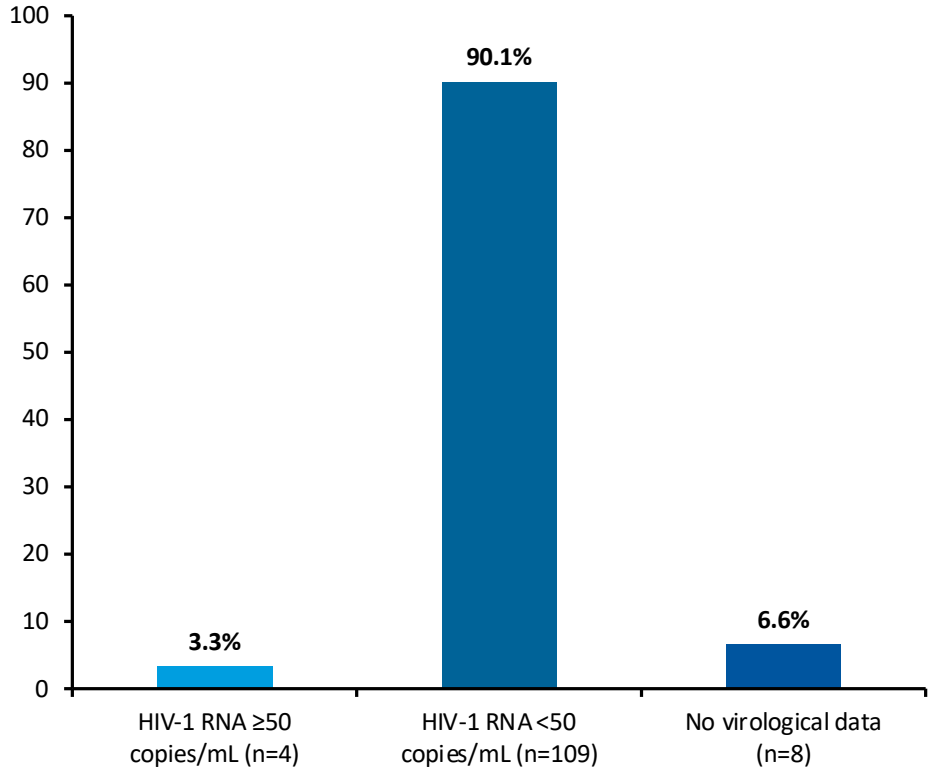
Past 3TC resistance: confirmed by genotypic testing or suspected based on prior virological failure while receiving XTC

No prior integrase resistance

CD4+ >200 cells/mm3

Sanger proviral DNA sequencing at screening without 3TC resistance mutations

	All (n=121)
Years since HIV diagnosis, median (IQR)	26.9 (20.7, 30.7)
CD4+ count (cells/mm3), median (IQR)	
Nadir	180 (71, 270)
Baseline	675 (516, 819)
ART duration (years), median (IQR)	23.4 (17.5, 27.1)
Number of previous ART regimens, median (IQR)	8 (6, 12)
Suppressed plasma HIV RNA (years), median (IQR)	9.2 (3.7, 14.4)
Confirmed prior 3TC resistance (%)	114 (94.2%)
M184V mutation (%)	107 (88.4%)
M184I/undefined (%)	7 (5.8%)
Prior K65R mutation (%)	5 (4.1%)
Suspected prior 3TC resistance (%)	**7 (5.8%)**



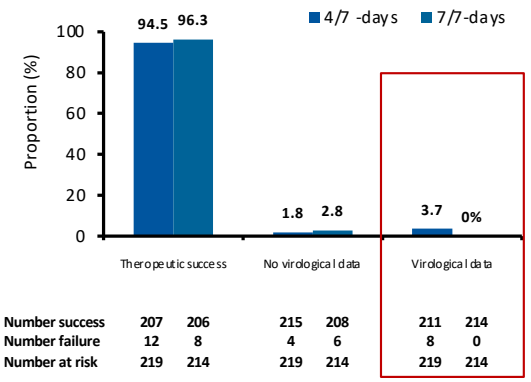
No treatment-emergent resistance was observed

De Miguel R, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. eP.A.097.

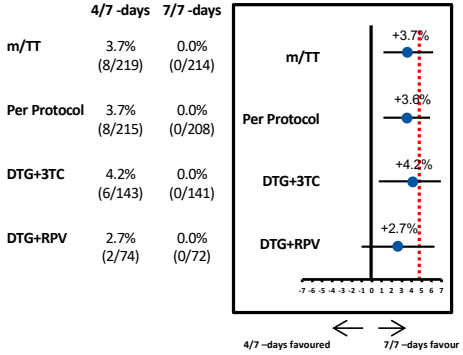
DUETTO: Maintenance Antiretroviral Dual Therapy Taken 4 Consecutive Days per Week Versus Dual Therapy 7/7 Days per Week

	Total N= 433	4/7- days N= 219	7/7- days N= 214
Age (years)	53 (46-61)	53 (44-61)	55 (48-61)
Gender, n (%)			
Female	83 (19.2)	39 (17.8)	44 (20.6)
Male	350 (80.8)	180 (82.2)	170 (79.4)
Route of HIV infection, n (%)			
MSM	263 (60.7)	141 (64.4)	122 (57.0)
Heterosexual	141 (32.6)	66 (30.1)	75 (35.1)
Other	29 (6.7)	12 (5.5)	17 (7.9)
Geographical origin, n (%)			
European	309 (71.4)	157 (71.7)	152 (71.0)
Sub-Saharan African	71 (16.4)	39 (17.8)	32 (15.0)
Other	53 (12.2)	23 (10.5)	30 (14.0)
Number of years since HIV diagnosis	15.1 (8.6-25.8)	14.8 (8.9-25.3)	16.0 (8.5-26.5)
Number of years since ART initiation	12.4 (7.8-22.4)	11.7 (7.6-20.6)	13.1 (8.1-22.9)
Duration of suppressed viremia (years)	9.7 (6.0-14.8)	9.8 (6.0-14.6)	9.3 (6.2-15.1)
History of previous virological failure, n (%)	105 (24.5)	45 (20.8)	60 (28.3)
History of AIDS defining events, n (%)	71 (16.4)	37 (16.9)	34 (15.9)
Number of months on Baseline ART regimen	27.4 (14.2-42.1)	26.0 (13.9-40.6)	27.9 (14.7-43.6)
Baseline ART regimen, n (%)			
DTG/3TC	284 (65.6)	143 (33.0)	141 (32.6)
DTG/RPV	146 (65.6)	74 (17.1)	72 (16.6)
DRV/r/3TC	3 (0.7)	2 (0.9)	1 (0.5)
CD4 nadir	276 (156-395)	290 (156-395)	267 (156-397)
CD4 cell count	688 (540-877)	688 (550-886)	678 (524.5-865)
CD8 cell count	645 (493 – 890)	645 (493-937)	649 (502.5-875)
CD4/CD8 ratio	1.1 (0.8 – 1.4)	1.1 (0.8-1.4)	1.0 (0.8-1.4)

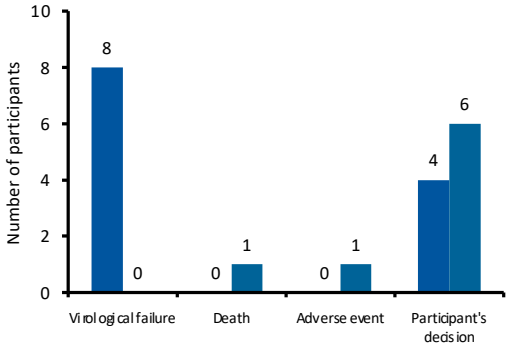
Primary endpoint (FDA snapshot method)



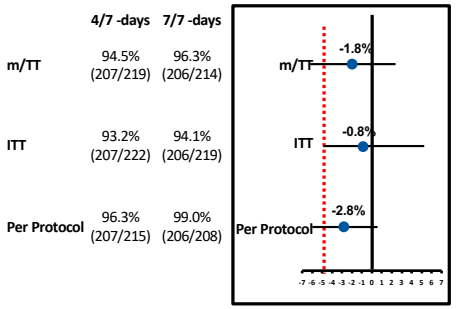
Virological failure (FDA snapshot method)



Reason for non-success of treatment



Therapeutic success (FDA snapshot method)



At W48, VF was observed in 8/219 (3.7%) in the 4/7-days and 0/214 in 7/7-days groups.
Resistance in 4 patients

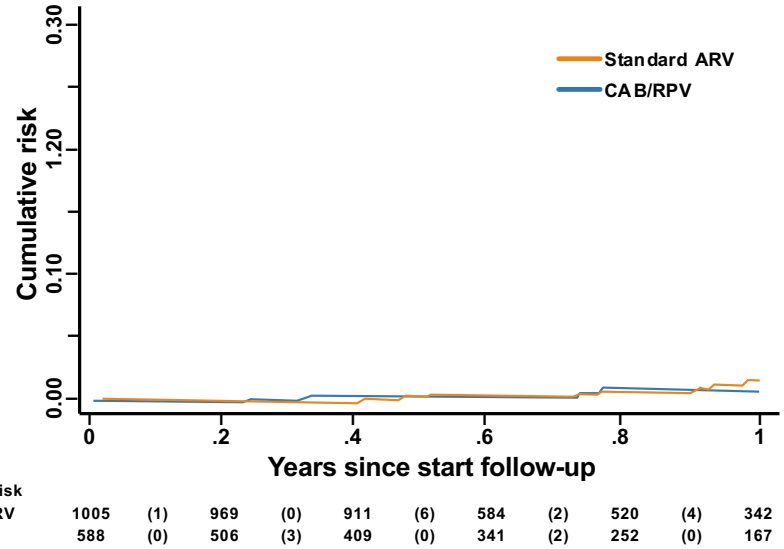
Landman R, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. eP.A.106.
DTG=3TC: Dolutégravir=Lamiduvine, DTG=RPV: Dolutégravir=Rilpivirine, DRV/r=3TC: Darunavir=Lamiduvine

Effectiveness of Injectable Long-Acting Cabotegravir and Rilpivirine for the Treatment of HIV-1: Results From the Dutch ATHENA National Observational Cohort

	Cases (n=619)		Controls (n=1,238)		
	n	%	n	%	p-value
Age, median [IQR]	444	[35-54]	46	[35-55]	0.017
Male	558	90%	1,116	90%	1.00
MSM	470	76%	947	76%	0.779
Years since start ART, median [IQR]	8.7	[5.8-13.4]	8.7	[5.9-13.4]	0.83
Nadir CD4, median [IQR]	320	[200-510]	330	[200-510]	0.64
CD4 at start follow-up, median [IQR]	730	[550-930]	770	[581-987]	0.009
HIV subtype A1A6	3	0.5%	4	0.3%	0.59
BMI > 30kg/m2	940	15%	136	11%	0.009
Known RPV associated mutations	0	0%	0	0%	N/A

- Median follow-up time 0.8 years [IQR 0.5-1.1]
  - Cases 0.7 years [IQR 0.3-1.1]
  - Controls 0.9 years [IQR 0.5-1.07]
- 58 (9%) cases discontinued long-acting CAB/RPV

- 5/588 (0.9%) of cases experienced virological failure
  - 2 failed with INI & NNRTI mutations* (see presentation Prof. Wensing)
    - Patient #1. INI: 155H RT: 101E+138K+230L
    - Patient #2: INI 138K+148R RT: 101E+138K



Jongen V, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS8.O1

Failure Following Switch From Long-Term Suppressive Oral ART to Long-Acting Cabotegravir/Rilpivirine Injections

universitätbonn

ukb universitäts klinikumbonn

We observed failure in 5 individuals switching from long-term suppressive oral ART to CAB/RPV LAI in the presence of only 1 or no risk factors

Case	Oral lead in	Rebound Months	Viral load cp/mL	Integrase profile	RT profile	CAB level mg/l	RPV level mg/l
A	Yes	9 m	15.000	138K, 148R	101E, 138K	2,5	0,005
B	No	3 m	830.000	-	101E, 103R, 179D, 181C, 189I	0,42	0,033
C	Yes	8 m	9400	140CS, 148R	101E	0,89	0,038
D	Yes	4 m	260/610.000	155H	101E, 138K, 230L	0,26	0,02
E	yes	13 m	630	138K, 148K	90I, 106A, 138K	1,4	0,02

- **All cases were adherent to LAI**
- **No relevant drug-drug interactions were observed**

Reference values	Cabotegravir mg/L	Rilpivirine mg/L
Protein adjusted IC90	0,166	0,012
ANRS Guidance level Q1	1,12	0,032
Mean population C_{trough} level	1,6	0,042

What happened?

A. BMI increase to 33.5 kg/m2
B. Missed injection? No lead in
C. High BMI, but only abdominal obesity
D. NNRTI exposure, but no NNRTI failure
E. Very high BMI, long needles used

Wensing A, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS8.O3.

Resistance Analysis of Long-Acting Lenacapavir in Heavily Treatment-Experienced

Category, n (%)	CAPELLA (N=72)
Resistance analysis population	27 (38)
LEN RAM emergence	14 (19)

Outcome After VF	VF participants with LEN RAMs (n=14)	
	Non-adherence to OBR (had at least 1 fully active agents)	Suboptimal OBR (had no fully active agents)
Resuppressed	1. Q67H 2. K70N + N74K 3. M66I + K705 4. N74D 5. Q67H	11. M66I + Q67H + N74D + A105T 12. M66I + T107A With OBR Change
Did not resuppress	6. M66I + N74D + A105T 7. Q67H + K70R + A105T 8. Q67K + K70H 9. Q67H + K70R + T107N 10. Q67H + K70R	13. M66I + A105T 14. M661 + Q67H + K70R + T107C

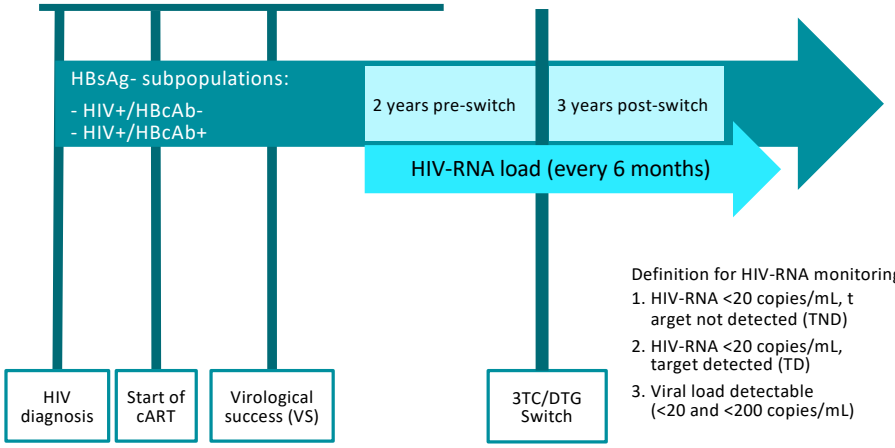
- Post VF, 7 of 14 participants with LEN RAMs achieved HIV-1 RNA <50 c/mL on LEN + OBR
- Most LEN RAMs were associated with strong reduction in replication capacity
- Some participants with LEN RAMs resuppressed upon resumption of OBR or with an OBR change

Margot N, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS8.O4.
LEN, lenacaoavir; OBR, optimized background regimen; RAM, resistance-associated mutation; VF, viroligic failure.

» HIV and Coinfections

HBcAb Positivity Is a Risk Factor for Failure to Achieve Complete Virological Suppression of HIV-RNA After Antiretroviral Switch to 3TC + DTG

» **Study design: European, multicentre retrospective study to investigate the impact of HBcAb positivity in PLWH undergoing switch to 2DR therapy with 3TC/DTG**



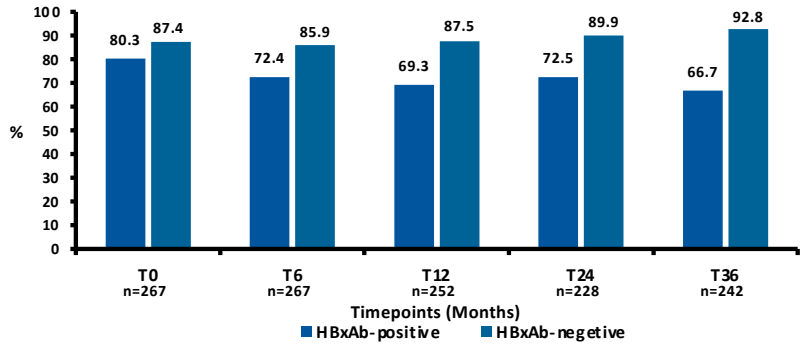
Endpoint: To assess differences in virological suppression efficacy between HBcAb+ vs HBcAb- subpopulation during follow up after therapeutic switch to 3TC/DTG

Results: HBcAb-positive vs HBcAb-negative

	HBcAb+ (n=76)	HBcAb- (n=191)	p
HIV RNA 24 months pre-2DR switch, n(%):			0.35
<20 cp/ml TND	49 (68.1%)	132 (76.7%)	
<20 cp/mL TD	13 (18.1%)	18 (10.5%)	
>20 and <50 cp/mL	10 (13.9%)	22 (12.8%)	
HIV RNA 12 months pre-2DR switch, n (%):			0.30
<20 cp/ml TND	58 (76.3%)	161 (84.7%)	
<20 cp/mL TD	4 (5.4%)	10 (5.4%)	
>20 and <50 cp/mL	14 (18.4%)	19 (9.9%)	
HIV RNA at 2DR switch, n (%):			0.15
<20 cp/mL TND, n (%)	61 (80.3%)	167 (87.4%)	
<20 cp/mL TD	8 (10.5%)	18 (9.4%)	
>20 and <50 cp/mL	7 (9.2%)	6 (3.2%)	

No differences in HIV-RNA suppression prior to switch to 3TC/DTG between the two subgroups

HIV-RNA <20 cp/ml TND post 3TC/DTG switch

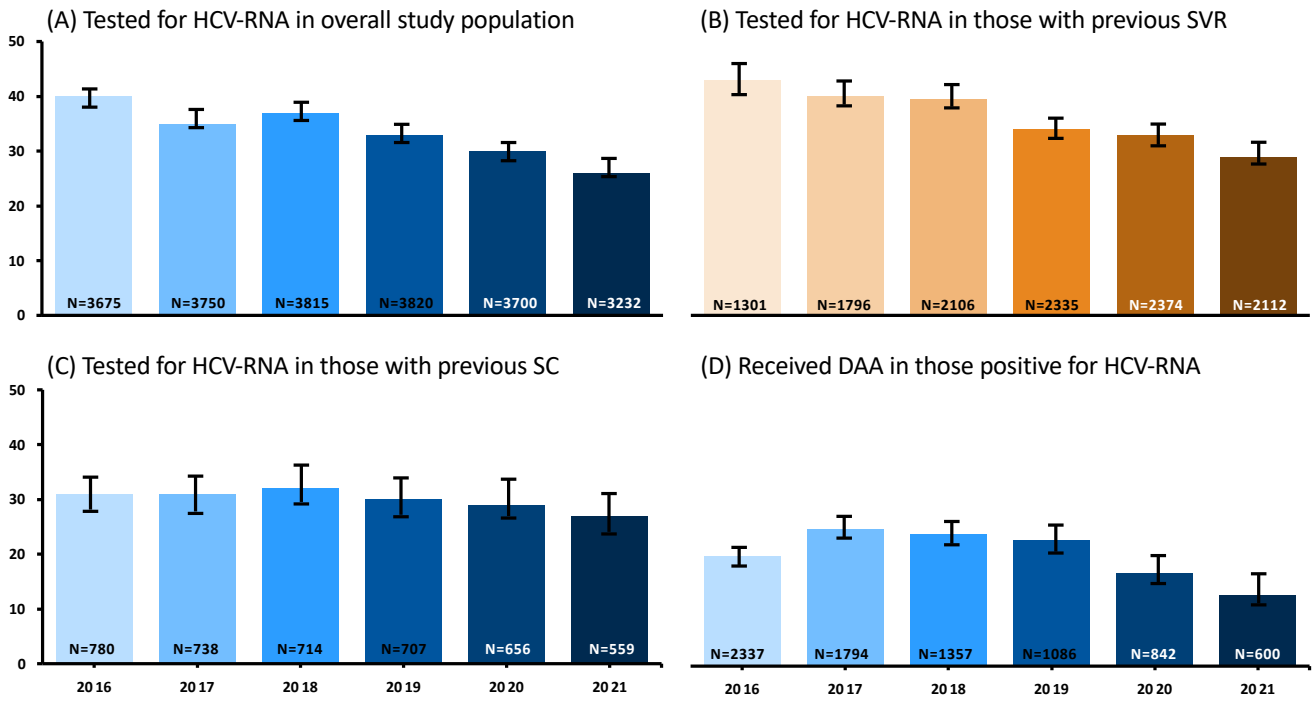


Malagnino V, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. RA2.O7.

Disruptions in Testing and Treatment Services for Hepatitis C Virus During the Sars-Cov-2 Epidemic Among Individuals With HIV Susceptible for HCV Reinfection: Results From the Eurosida Study

- **Objective: To determine the effect of the SARS-CoV-2 epidemic on HCV testing and commencing anti-HCV treatment in PWH across Europe**
- **Methods: Prospective, longitudinal cohort study**
- **Inclusion criteria: Participating between Jan 2016 and Dec 2021 and having a positive anti-HCV antibody test (i.e., susceptible for HCV re-infection and eligible for HCV-RNA testing)**

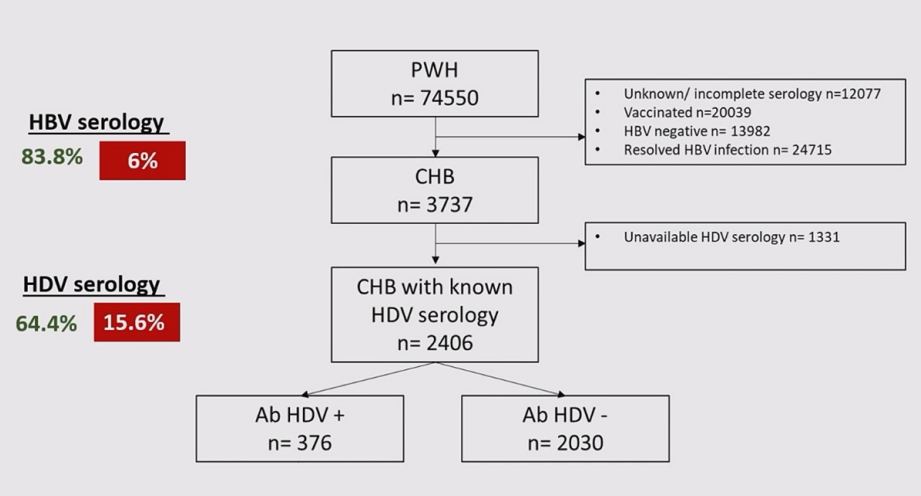
Testing for hepatitis C virus (HCV) RNA and commencing direct acting antivirals (DAA) during 2016-2021



Boyd A, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. RA3.O6.

Hepatitis delta in France

- **Objective:** To evaluate prevalence, incidence, and risk factors for HDV infection in a nationwide cohort from France



HDV prevalence

- Global **15.6%**
- IVDU **56.5%**
- HCV coinfection **42.4%**

Factors associated with HDV infection

	Multivariate analysis	
	OR (95% CI)	*p* value
Gender		
Male	**1.53** (1.08-2.18)	0.02
Country of origin		
Africa	**2.80** (1.73-4.54)	<0.001
Eastern Europe	**3.25** (1.56-6.77)	0.002
HIV risk factor		
Heterosexual	**1.82** (1.11-2.99)	0.02
IVDU	**7.05** (3.89-12.78)	<0.001
HCV coinfection	**2.81** (1.72-4.60)	<0.001

HBV, hepatitis B virus; ***HCV,*** hepatitis C virus ***HDV,*** hepatitis D virus; ***IVDU,*** intravenous drug use

HDV incidence

(superinfection)

- Consecutive serologies available for **n=1827** persons (follow-up 21006 PY)
- **27** HDV superinfections
- **HDV incidence rate 0.12/100 PY** (95% CI 0.008-0.18)
- **Incident HDV : older age** at HDV diagnosis (48,0 years vs 37,3 years, p<0,001)

Alfaiate D et al. EACS 2023

Clinical Manifestations of Monkeypox (Mpox) And Impact of Vaccination in People With and Without HIV in Catalonia. A Population-Wide Study

Objective: To study differences in clinical outcomes between PWH and without.

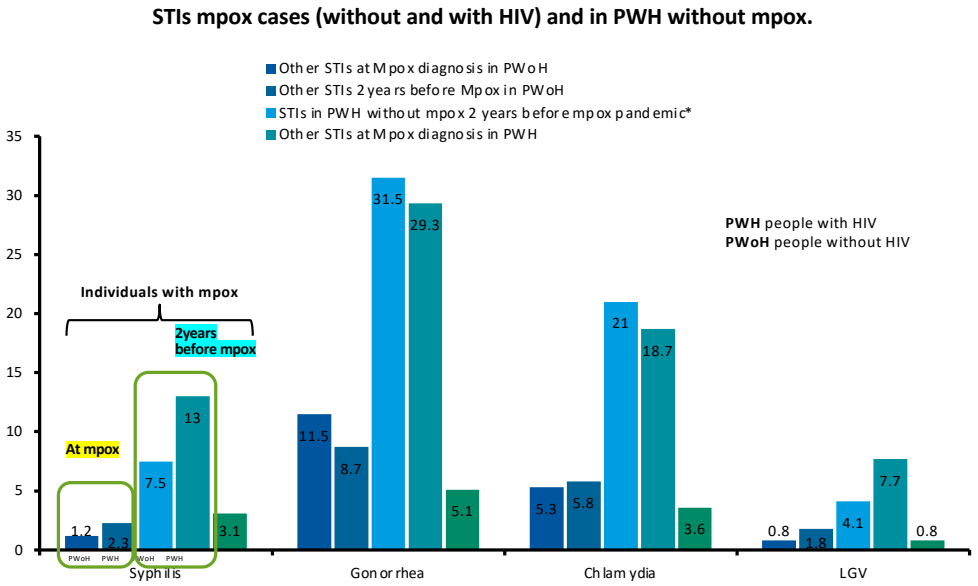
CLINICAL OUTCOME IN PEOPLE **WITH AND WITHOUT HIV**

Skin bacterial infections
Corneal infections
Pnemonia
Proctitis
Hospitalization Sepsis
Encephalitis
Death

A significant decline in the mpox incidence was observed after vaccination (p<0.0001)

	Mpox in PWoH N=1280	Mpox in PWH N=842	p-value
Age, years (median (IQR))	36 (90-43)	40 (34-46)	<0.001
Male, n (%)	1229 (96.1)	840 (99.8)	<0.001
Origin, n (%)			
Spanish	756 (59.1)	438 (32.0)	0.001
European	192 (15.0)	113 (13.4)	0.31
South American	245 (19.1)	259 (30.8)	<0.001
Other	87 (6.8)	32 (3.8)	0.003
Asymptomatic, n (%)	62 (4.8)	20 (2.4)	0.004
Symptoms, n (%)			
Fever	641 (50.1)	467 (55.5)	0.015
Asthenia	394 (30.8)	243 (28.9)	0.35
Odynophagia	268 (20.9)	201 (23.9)	0.11
Myalgia	251 (19.6)	150 (17.8)	0.30
Headache	303 (23.7)	164 (19.5)	0.023
Generalized lymphadenopathy	153 (12.0)	94 (11.2)	0.58
Localized hymphadenopathy	530 (41.1)	346 (41.1)	0.89
Anogenital exanthema	727 (56.8)	472 (56.1)	0.74
Oro-facial exanthema	338 (26.4)	239 (28.4)	0.32
Exanthema in other localization	509 (39.8)	393 (46.7)	0.002
Type of exanthema			
Maculopapular	181 (14.1)	129 (15.3)	0.45
Vesicular	308 (24.1)	185 (22.0)	0.26
Pustular	237 (18.5)	194 (23.0)	0.011
Umbilicated	194 (15.2)	95 (11.3)	0.011
Crusts	127 (9.9)	83 (9.9)	0.96
Hemorrhagic	4 (0.3)	3 (0.4)	0.86
Complications*, n (%)	57 (4.5)	50 (5.9)	0.13
Skin bacterial infections	22 (1.7)	15 (1.8)	0.91
Localizations:			
Ano-genital	9 (34.6)	6 (42.9)	
Face	9 (34.6)	2 (14.3)	
Limbs	4 (15.4)	1 (7.1)	
Oral	4 (15.4)	5 (35.7)	
Corneal infections	5 (0.4)	3 (0.4)	0.9
Pneumonia	0	2 (0.2)	0.081
Proctitis	15 (1.2)	14 (1.7)	0.34
Hospitalization	22 (1.7)	22 (2.6)	0.16
ICU	1 (0.1)	0	0.42
Sepsis	0	0	
Encephalitis	0	0	
Death	0	0	
Other	3 (0.2)	0	
Long term complications	74 (9.3)	65 (12.3)	0.085

PWoH: people without HIV
PWH: people with HIV



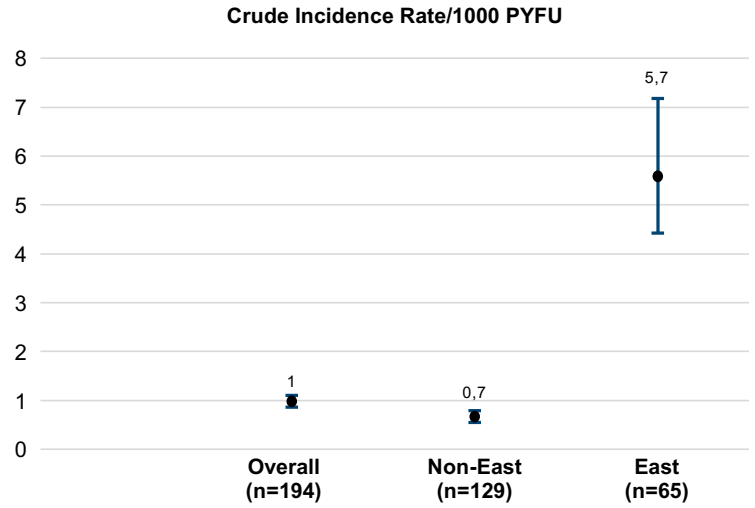
Overall, 16.5% of mpox cases were diagnosed with a concomitant STI and 43% had at least one notifiable STI in the 2 years before mpox compared to 8.5% of PWH without mpox.

Martin-Iguacel R, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS11.O1.

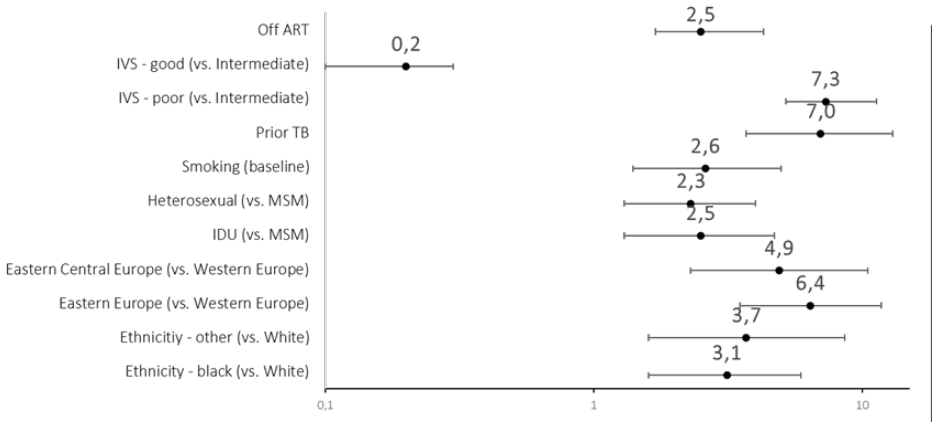
Modifiable Risk Factors and Their Population Attributable Fractions for TB in PWH Across Europe (Respond-Cohort)

» **A total of 35.332 PWH were included. Overall, 194 TB cases during 197.734 PFYU of which 129 TB cases during 186.424 PFYU were from non-Eastern regions and 65 TB cases during 11.309 PFYU from Eastern Europe**

TB incidence rate/1000 PYFU



Risk factors for TB - overall



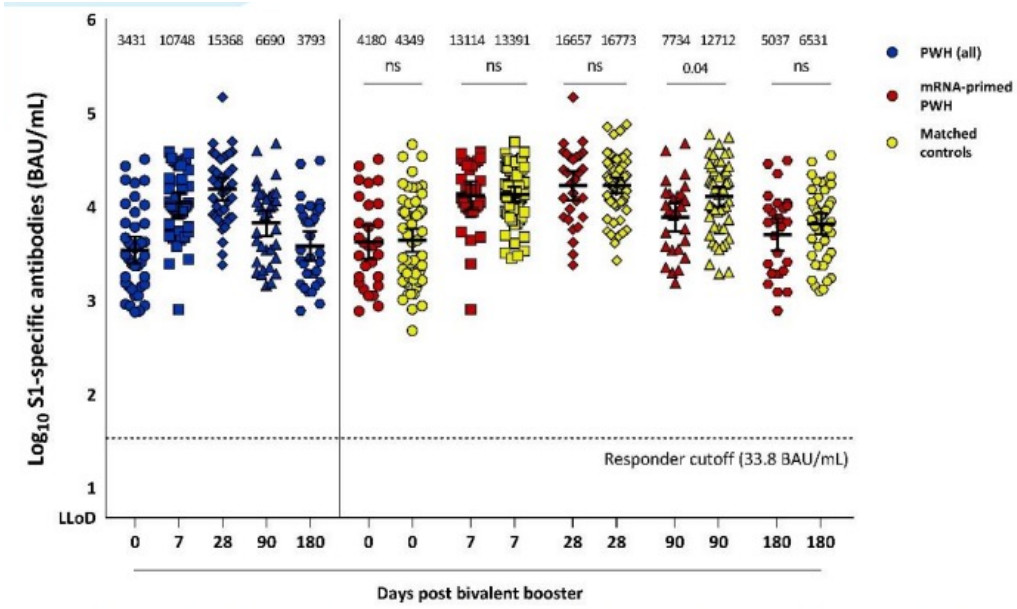
IVS: immunological-virological suppression

Kraef C, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. OS2.O5.

Immunogenicity of a bivalent Omicron BA.1 COVID-19 booster vaccination in PWH in the Netherlands

- **Study objective:** To evaluate the immunogenicity of a bivalent Omicron BA.1 booster vaccination PWH compared to matched controls without HIV.
- **Methods:** Participants ≥45 years received mRNA-1273.214 and <45 years BNT162b2 BA.1 according to national regulation
- **Results:** Overall, 40 PWH and 58 healthy controls were included into the study. 39/40 (98%) had a HIV-RNA <50 copies. The median CD4+ T-cell count was 775/µl (511 – 965). No differences were found when comparing the progression of S1-specific antibodies over time between the matched groups (p=0.82).

Detection of (ancestral) S1-specific binding IgG antibodies at baseline before bivalent booster (day 0, as indicated by circles), and at day 7 (squares), 28 (diamonds), 90 (triangles), and 180 (hexagons) post-booster in all PWH (N=40) (left panel) and in propensity score-matched PWH (N=29) and controls (N=58) (right panel).



Jongkees MJ, et al., EACS 2023, eposter B2.053

» HIV and Comorbidities

Efficacy and safety of bariatric surgery in PWH: a retrospective matched cohort analysis

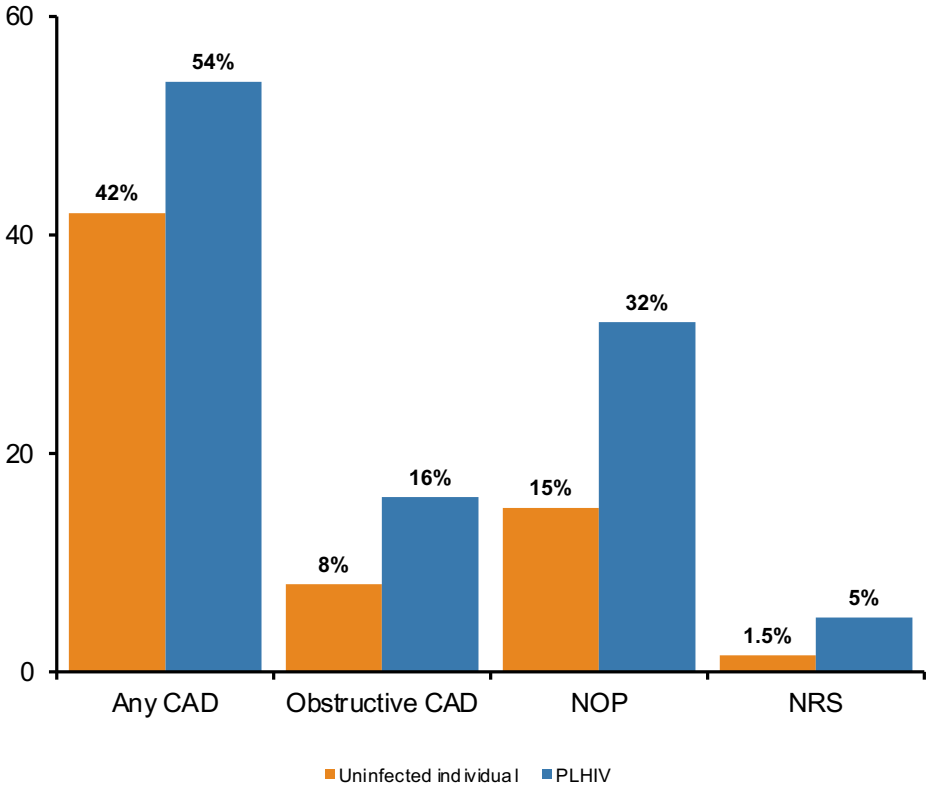
- 27 PWHIV and 168 Matched Controls With a Baseline Median Baseline BMI at Approximately 41 Kg/m2

Total weight loss at 1 and 2-years post-surgery

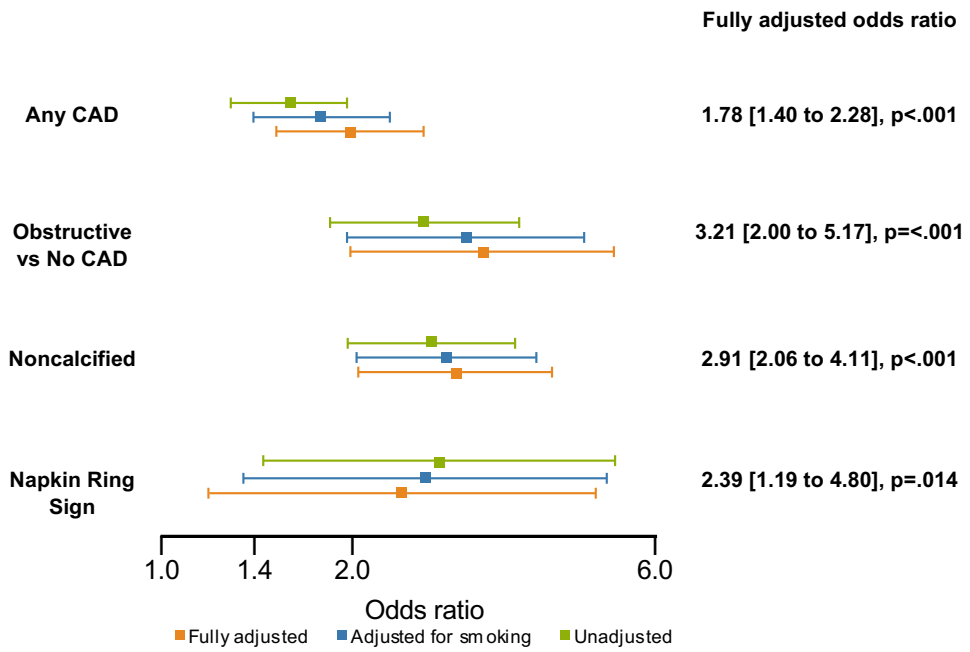
Cohort	1-year post-surgery		2-years post-surgery	
	≥20% TWL, n(%)	OR (95% CI)	≥20% TWL, n(%)	OR (95% CI)
People living with HIV	24 (89%)	0.5 (0.13 – 2.0)	22 (81.5%)	0.5 (0.2 – 1.4)
Uninfected Controls	158 (94%)	Reference	154 (91.7%)	Reference

Zino L, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. eP.C3.005.

Copenhagen HIV Cohort: Coronary plaques in HIV+ (n=519) vs HIV- (n=1114)



Association between HIV and coronary artery disease



Statistical analyses were adjusted for age, sex, smoking, hypertension, dyslipidemia, diabetes, and overweight/obsity

Knudsen A, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS4.O3.

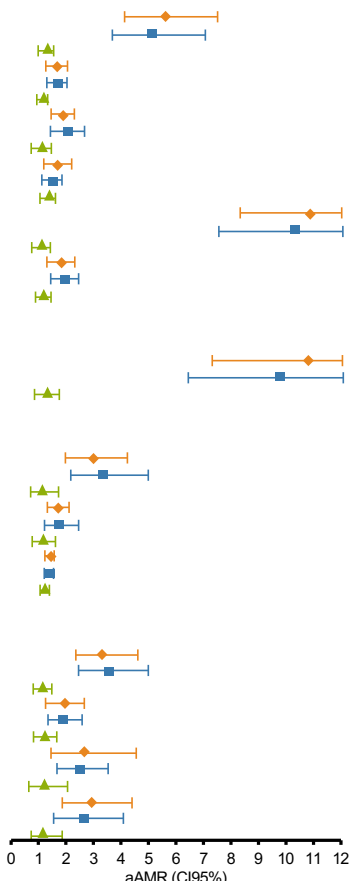
Effect of pLLV on Inflammatory and Adhesion Molecule (n=27 per group)

No significant difference were observed between both PWH groups

Only the LLV group showed a significant increase in IL-13 over the non-HIV controls. Critical mediator in allergy, asthma and CVD. (Quan N et al. (2021)

Similar increase in inflammatory and Th1/Th2-related cykokines, chemokines and growth factors were observed in both PWH groups compared to NHC

Comparison of levels of inflammatory biolmarkers between the three groups of study. This figure summarizes only the statistically significant biomarkers for any of the three comparisons (*, p(0.05, q<0.15)



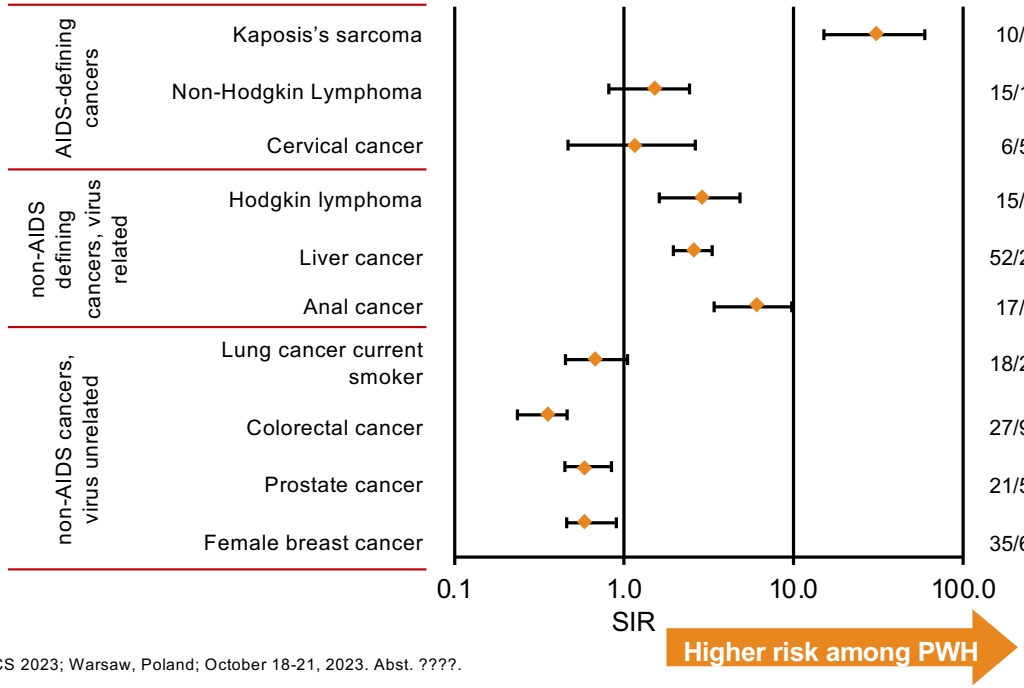
Th1/Th2 response	aAMR (CI95%)	p value	q value
IFNG	5.43 (4.01-7.36)	<0.001*	<0.001*
	4.96 (3.57-6.89)	<0.001*	<0.001*
	1.11 (0.89-1.39)	0.368	0.948
IL4	1.46 (1.12-1.89)	0.007*	0.026*
	1.47 (1.15-1.88)	0.003*	0.014*
	0.98 (0.79-1.2)	0.819	0.948
CXCL8	1.68 (1.3-2.18)	<0.001*	0.002*
	1.82 (1.3-2.55)	0.001*	0.005*
	0.93 (0.66-1.3)	0.658	0.948
IL 13	**1.49 (1.1-2.03)**	**0.014**	**0.045**
	1.28 (0.98-1.66)	**0.076**	**0.222**
IL18	10.72 (8.45-13.6)	<0.001*	<0.001*
	10.2 (7.47-13.92)	<0.001*	<0.001*
	0.01 (0.66-1.25)	0.567	0.948
TNF	1.64 (1.21-2.15)	0.001*	0.005*
	1.77 (1.37-2.3)	<0.001*	<0.001*
	0.99 (0.82-1.21)	0.939	0.961
Inflammatory cytokines			
IL6R	10.7 (7.31-15.65)	<0.001*	<0.001*
	9.67 (6.41-14.57)	<0.001*	<0.001*
	1.08 (0.76-1.55	0.665	0.948
Chemokine			
CCL11	2.77 (1.91-4.02)	<0.001*	<0.001*
	3.12 (2.03-4.79)	<0.001*	<0.001*
	0.9 (0.57-1.43)	0.655	0.948
CXCL10	1.51 (1.15-1.98)	0.005*	0.020*
	1.55 (1.08-2.22)	0.021*	0.074*
	0.97 (0.69-1.38)	0.881	0.948
CCL5	1.23 (1.07-1.41)	0.005*	0.021*
	1.19 (1.04-1.37)	0.015*	0.054*
	1.03 (0.92-1.15)	0.636	0.948
Growth factor			
BDNF	3.12 (2.19-4.44)	<0.001*	<0.001*
	3.35 (2.36-4.77)	<0.001*	<0.001*
	0.93 (0.65-1.32)	0.69	0.948
EGF	1.74 (1.21-2.5)	0.005*	0.020*
	1.67 (1.17-2.37)	0.007*	0.027*
	1.03 (0.73-1.44)	0.879	0.948
PDGFB	2.44 (1.35-4.43)	0.005*	0.020*
	2.29 (1.54-3.39)	<0.001*	0.001*
	1 (0.57-1.78)	0.987	0.948
VEGFA	2.7 (1.72-4.24)	<0.001*	0.001*
	2.43 (1.49-3.94)	0.001*	0.004*
	0.95 (0.54-1.67)	0.855	0.948

◆ LLV vs NHC
■ SV vs NHC
▲ LLV vs SV

Lara-Aguilar V, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. PS4.O1.

French Hospital Database: Changing Malignancy Risk vs General Population

Age standardized incidence ratios (SIR) in PWH with CD4 ≥ 500/mm3 for at least 2 years and controlled viral load (< 50 copies/mL) over 2008-2018



	Oc/E	Number of PY	Standardized incidence rates (95% CI)	Standardized incidence ratios
Kaposis's sarcoma	10/0.3	157 189	6.3[2.3-10.2]	27.9[13.3-51.4]
Non-Hodgkin Lymphoma	15/11.2	160 691	9.2[4.5-13.9]	1.3[0.7-2.1]
Cervical cancer	6/5.7	54 796	1.1[2.3-19.9]	1.0[0.4-2.3]
Hodgkin lymphoma	15/5.9	161 699	9.3[4.5-14.0]	2.6[1.4-4.2]
Liver cancer	52/23.2	162 440	32.6[23.7-41.4]	2.2[1.7-2.9]
Anal cancer	17/3.2	162 018	10.7[5.6-15.8]	5.3[3.1-8.5]
Lung cancer current smoker	18/29.9	25 789	59.5[33.4-85.6]	0.6[0.3-0.9]
Colorectal cancer	27/93.3	162 018	16.8[10.1-23.3]	0.3[0.2-0.4]
Prostate cancer	21/52.0	68 111	10.88[17.8-43.9]	0.4[0.3-0.6]
Female breast cancer	35/65.1	54 402	54.9[43.5-86.3]	0.5[0.4-0.81]

Grabar S , et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. ????.

Summary

- Eastern Europe and Central Asia remain the fastest growing HIV epidemic in the world.
- EACS and ECDC aim at raising the standards of HIV care and reducing the observed inequities in the standards of care in the European region.
- Fixed-dose doravirine/islatravir (100/0.75 mg) non inferior to continuation of BIC/F/TAF for maintenance of viral suppression. Decreases in lymphocytes. Waiting for the islatravir 0.25 mg clinical trial data.
- Real World Data: little difference between BIC/F/TAF and DTG/3TC as maintenance strategies
- After excluding lamivudine mutations in proviral DNA by population sequencing, DTG/3TC effectively maintained virological suppression in persons with HIV and prior history of 3TC resistance. No emergent resistance
- Dual ART 4 days a week not non-inferior to daily oral dual ART.
- Uptake of LA CAB RPV variable. Small risk of virologic failure
- Reasons for failure of LA CAB RPV in some cases unknown. Drug levels?
- Bariatric surgery similarly tolerated and effective in HIV+ (need PK, efficacy data)
- Declining rates of AIDS and viral cancers in PWHIV but prostate, breast and colorectal cancers (‘aging related’) rising. HD, anal, liver and KS all remain more common in PWHIV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