

SITA 23 NOVEMBRE 2023, PADOVA

La terapia nel paziente naïve: dai trials clinici alla real life

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Disclosure of potential conflicts of interest 2022-23

Consultancy for ViiV

Speakers' honoraria ViiV, Gilead

LA PRIMA ART

CROI 2023 OPENING SESSION

Life Expectancy for 21-Year-Old with HIV, 1980s and Today

1980s
(no ART)

1-2 years from
AIDS diagnosis

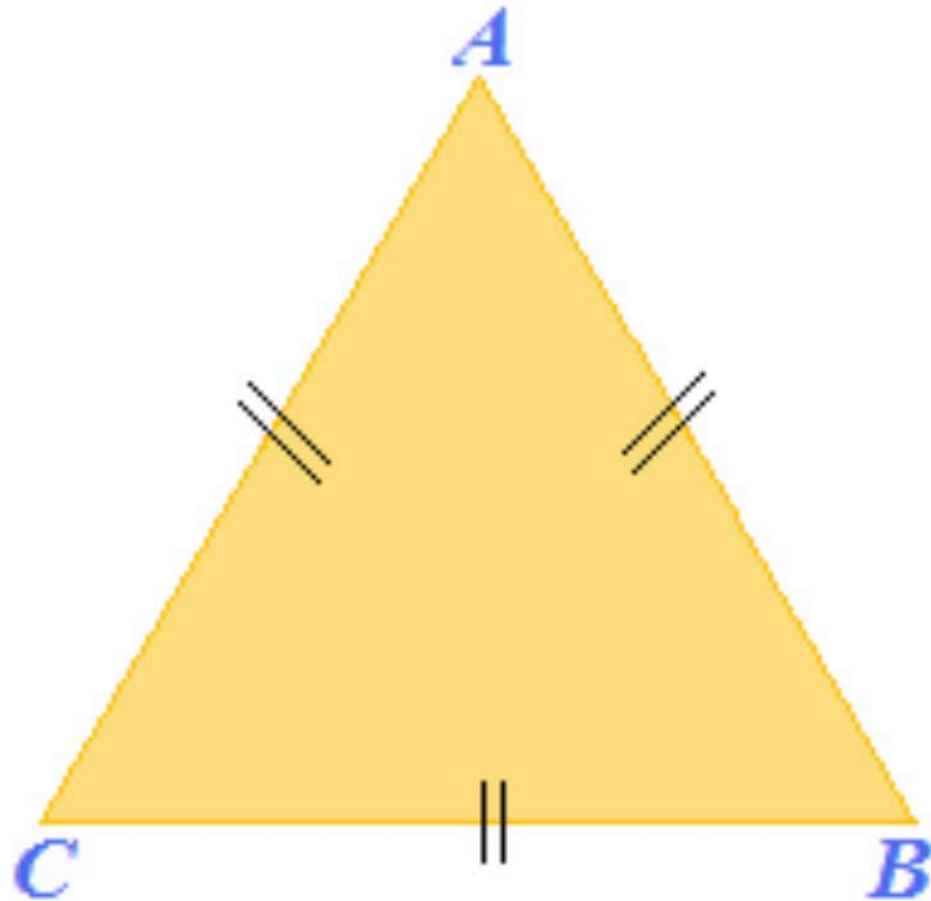
Today
(on ART)

~56
years

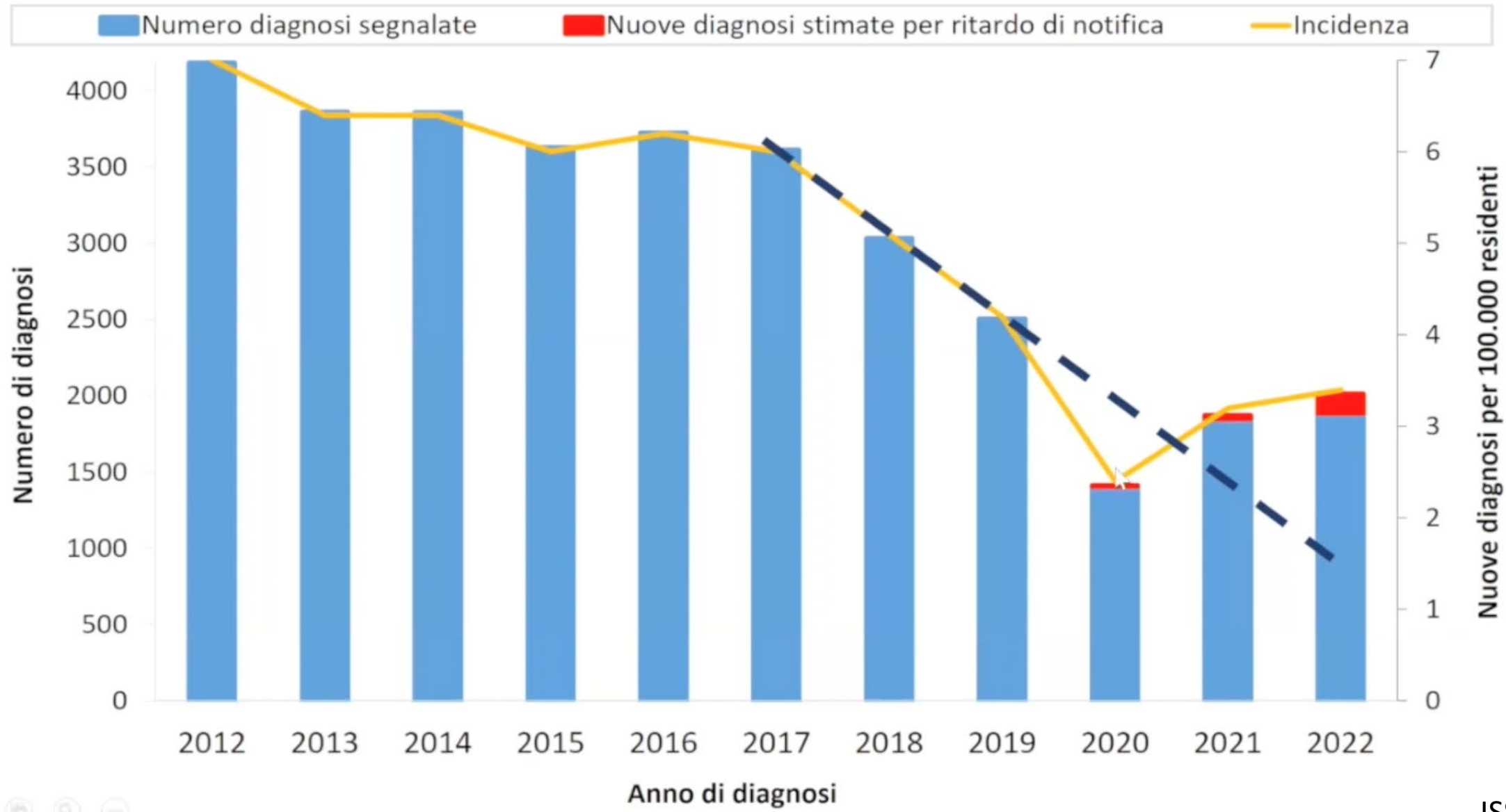
Source: JL Marcus et al. *JAMA Netw Open* 3:e207954, 2020.



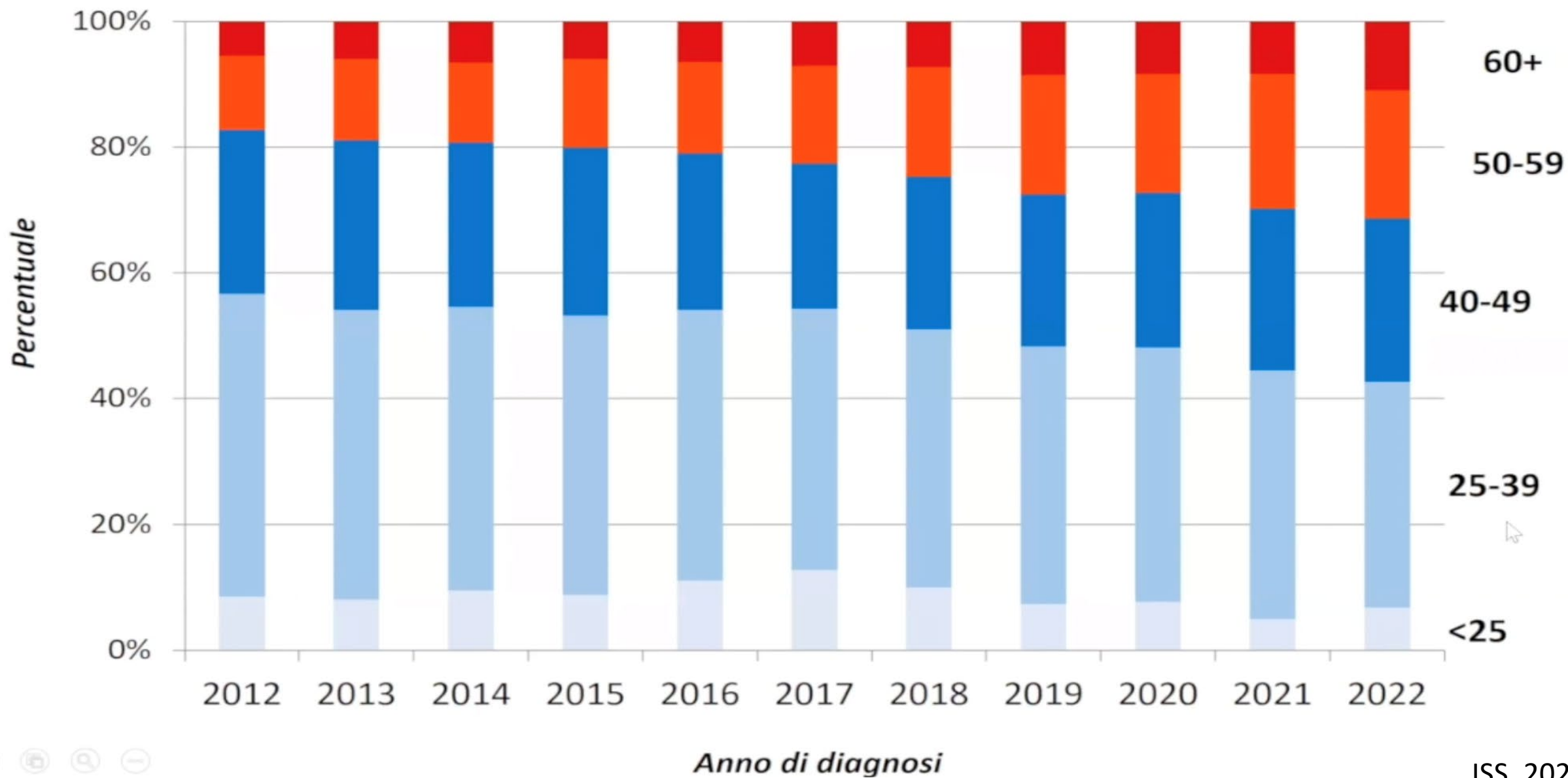
Individuo-Virus-Chemioterapico



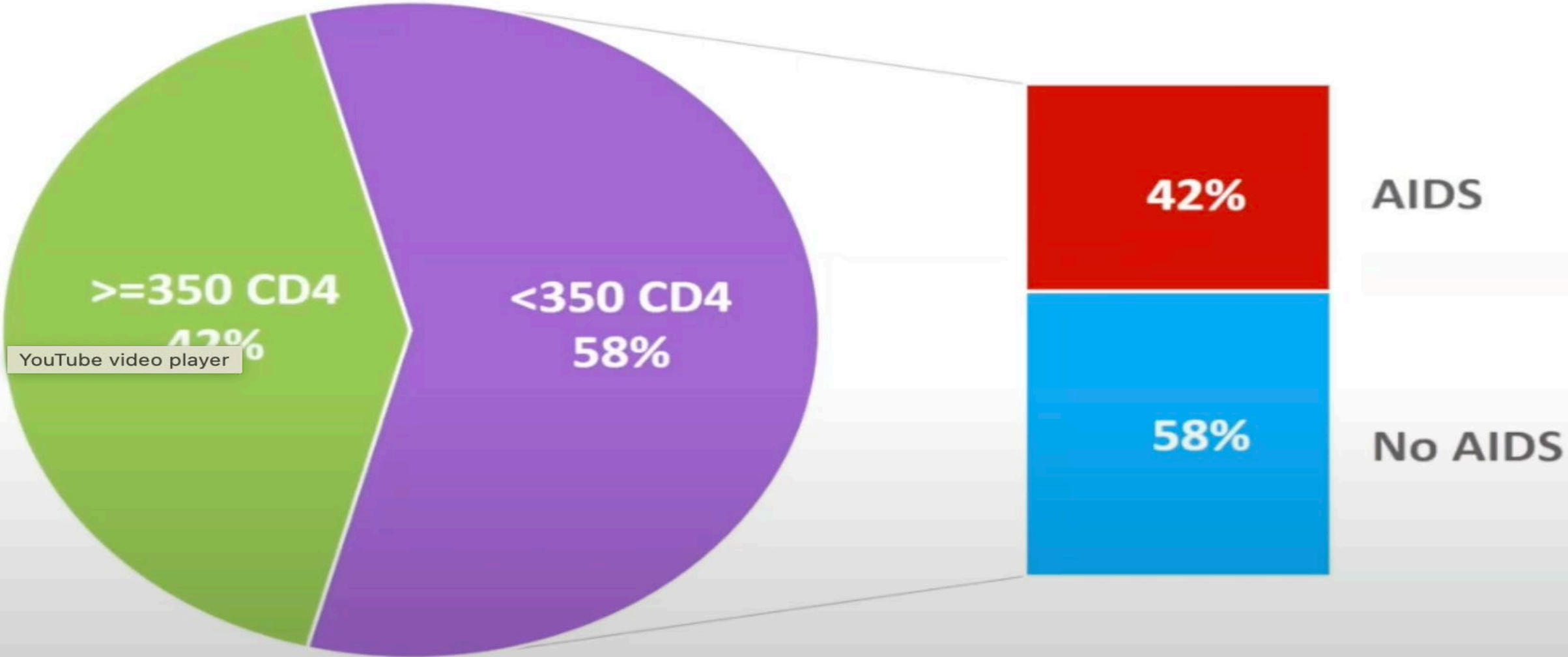
Trend in aumento dell'incidenza HIV post Covid



Aumenta la quota di nuove diagnosi in persone di 50+ anni



Più della metà sono late presenters (2022)



YouTube video player

CONCISE COMMUNICATION

Rising rates of recent preexposure prophylaxis exposure among men having sex with men newly diagnosed with HIV: antiviral resistance patterns and treatment outcomes

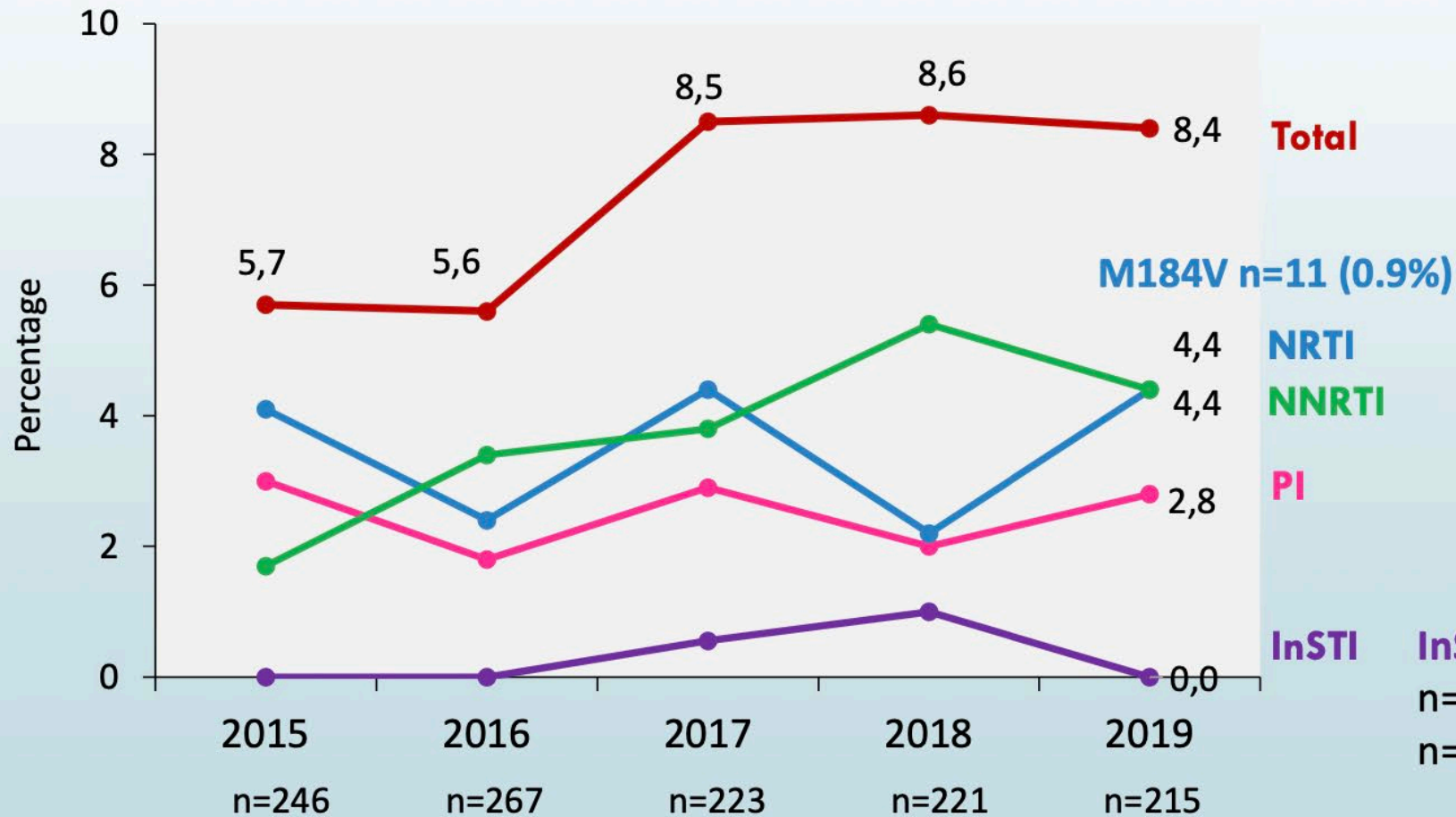
Nicolò Girometti^a, Sheena McCormack^{a,b}, Victoria Tittle^a, Alan McOwan^a, Gary Whitlock^a, on behalf of the 56 Dean Street Collaborative Group

- M184V mutation was harboured more commonly in the recent PrEP use group (30% vs. 1%, $P < 0.01$).
- The proportion of individuals recently exposed to PrEP among those diagnosed with HIV rose sharply, reaching 21% in the first semester of 2020.
- Viral suppression was achieved by all patients intensified from PrEP to antiretroviral treatment (ART) who remained in care at week 24.


Results: Fifty-two of 1030 (5%) individuals reported recent PrEP exposure at HIV diagnosis; 98% were MSM, median age 34 years (interquartile range [IQR] 28–42), 65% of white ethnicity, 65% non-UK-born. 35% reported PrEP intake the day before testing HIV positive, 46% reported sub-optimal PrEP adherence since their last negative HIV test result. Thirty-three of 52 (63%) were self-sourcing PrEP and 9/52 (17%) reported issues with its supply. Recent PrEP use was associated to lower HIV viral load and higher CD4⁺ cell count at baseline than in counterparts non-recently exposed to PrEP ($P < 0.01$). M184V mutation was harboured more commonly in the recent PrEP use group (30% vs. 1%, $P < 0.01$). The proportion of individuals recently exposed to PrEP among those diagnosed with HIV rose sharply, reaching 21% in the first semester of 2020. Viral suppression was achieved by all patients intensified from PrEP to antiretroviral treatment (ART) who remained in care at week 24.

Prevalence of major RAMs in recent HIV infection

High frequency variants (>20% frequency, n=1175 participants)



Samples collected at diagnosis (routine surveillance)
Recent infection (<4 months) by RITA algorithm*
91% Males, 74% MSM
72% White ethnicity
47% In London



*Strength of HIV-specific Ab-Ag binding by Limiting-Antigen Avidity Assay with OD index <1.5; CD4 count >200 cells; VL >1000 cps/mL

InSTI

InSTI RAMs

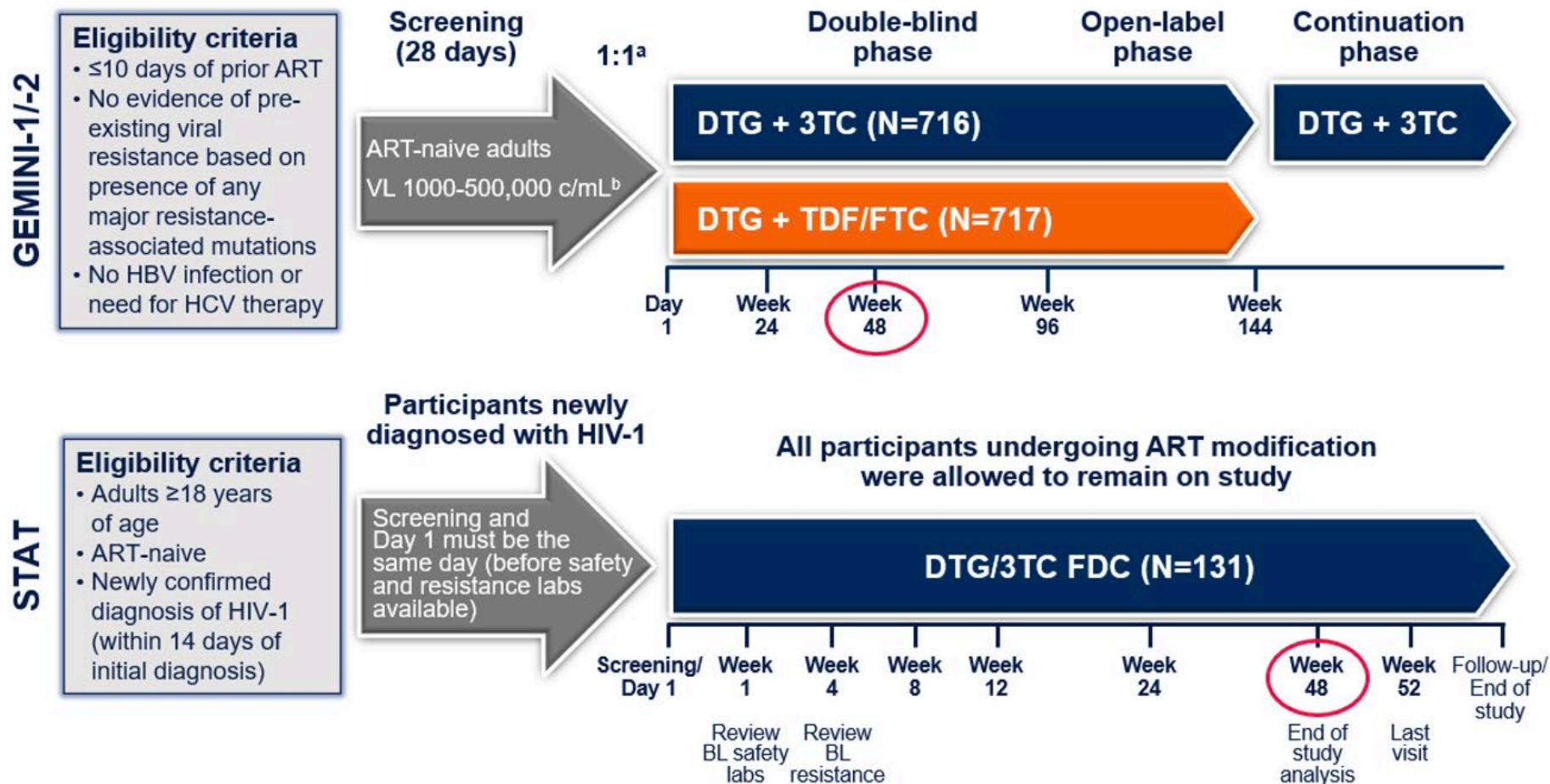
n= 1/180 in 2017 (E138K)

n= 2/187 in 2018 (E92G; E138K)

Table 5.1 Recommendations for choice of first-line ART (in alphabetical order by core agent)

Recommended as initial treatment for most people living with HIV (Grade 1A)	
Regimen	Specific details
Bictegravir/emtricitabine/tenofovir AF	
Dolutegravir plus emtricitabine/tenofovir AF or emtricitabine/tenofovir DX	Bone/renal caveats for tenofovir DX
Dolutegravir/lamivudine	No baseline lamivudine resistance Baseline viral load <500,000 copies/mL and CD4 count >200 cells/mm ³
	No active hepatitis B infection and if at risk of hepatitis B, hepatitis B virus immune
Dolutegravir/lamivudine/abacavir	HLA B*5701 negative and estimated 10-year risk of CVD less than 10%
Recommended as initial treatment in certain clinical situations (Grade 1A)	

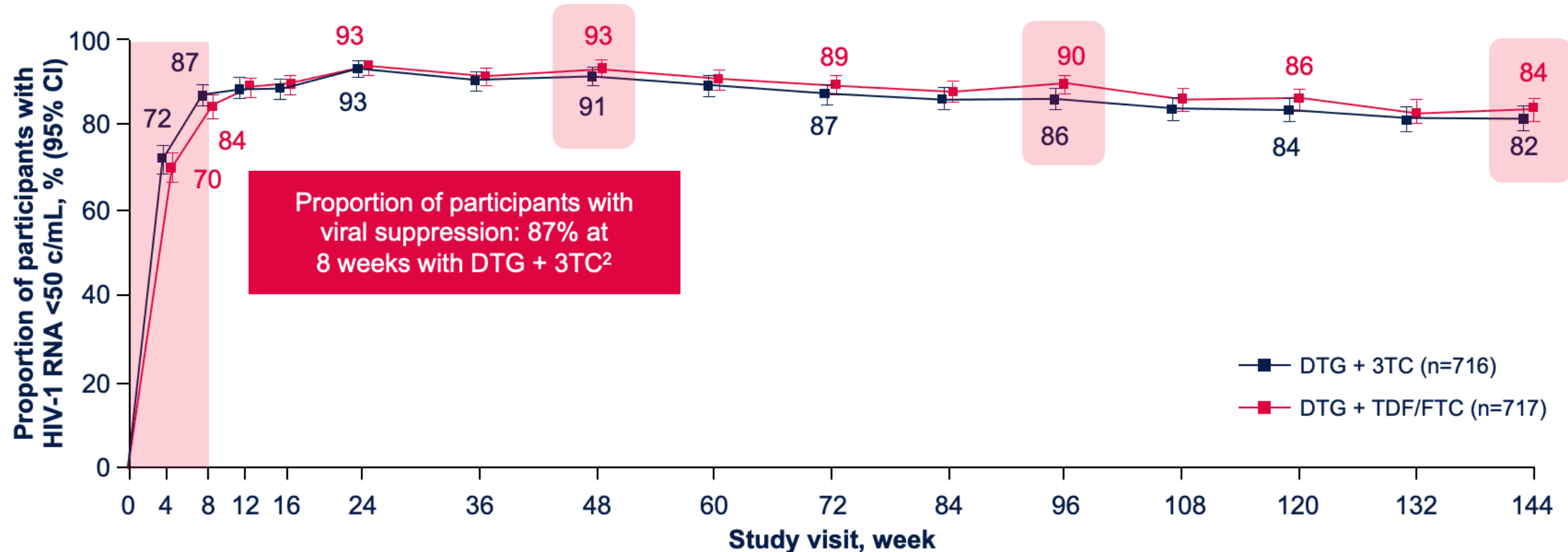
GEMINI-1/-2 and STAT: Study Designs



^aRandomization in GEMINI-1/-2 stratified by baseline plasma HIV-1 RNA (≤100,000 vs >100,000 c/mL) and CD4+ cell count (≤200 vs >200 cells/mm³). ^bParticipants with VL ≤500,000 c/mL at screening but >500,000 c/mL at baseline (Day 1) were allowed to continue the study.

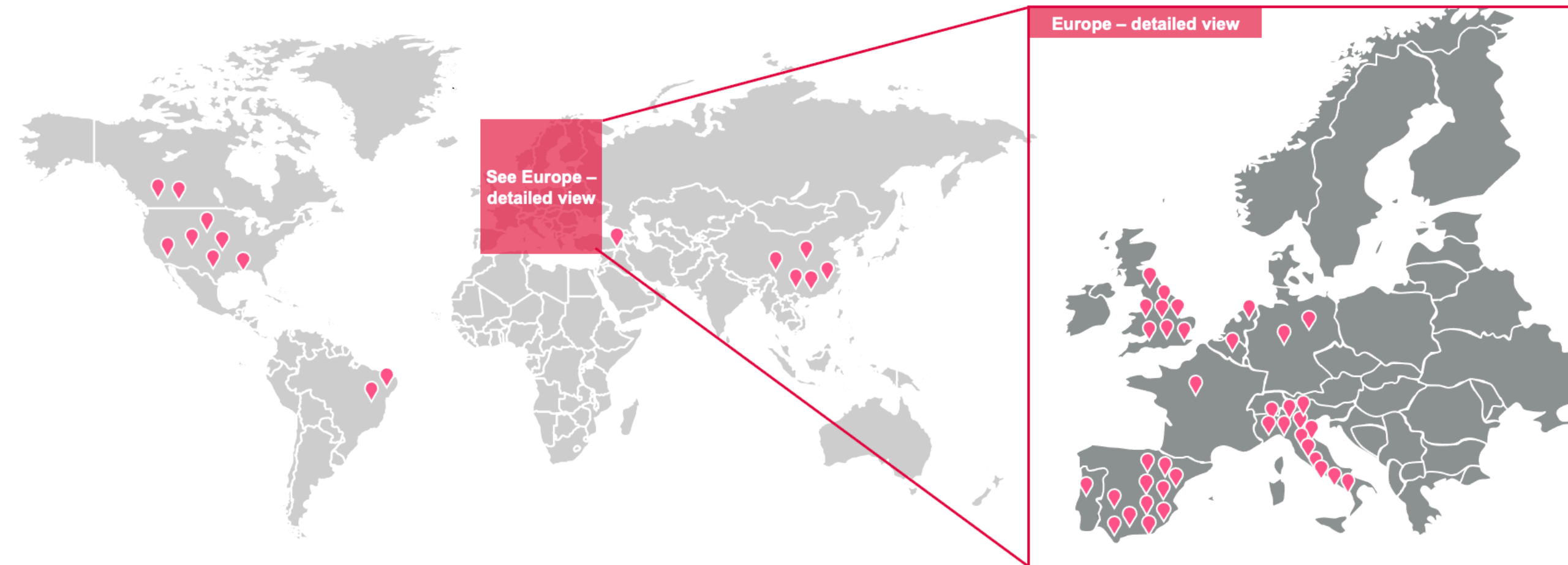
DTG + 3TC Has Demonstrated Rapid and Durable Efficacy in Treatment-naïve Participants Through 144 Weeks

GEMINI-1 and -2^{1,2}



A DTG-based 3DR did not deliver additional potency, speed or durability of antiviral efficacy versus DTG + 3TC

11,701 people worldwide have received DTG + 3TC in real-world cohorts



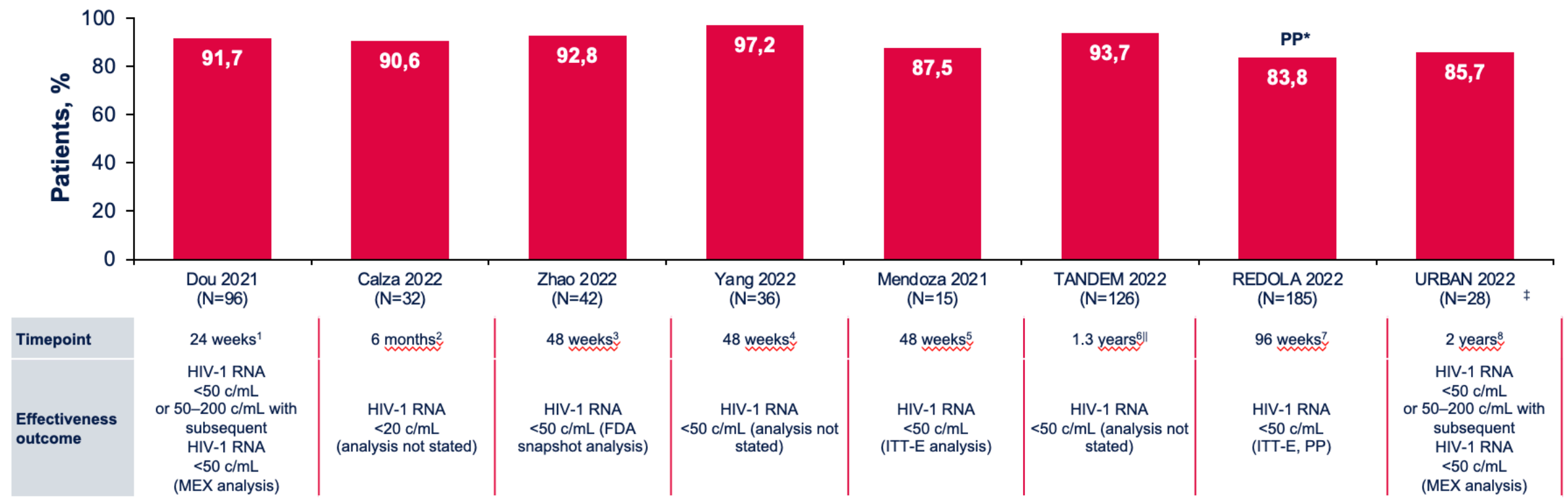
54
Consistent
with the EU label

Potential overlap between patient cohorts cannot be ruled out; map is accurate to the level of country of study, placement within country is for visual representation purposes only; *DTG + 3TC is indicated for HIV-1 infection in adults and

References: Nasreddine R, et al. HIV Med 2022;doi: 10.1111/hiv.13373 (and Suppl. Appendix); Pereira Goulart S, et al. EACS 2019. Poster PE2/34; Silva Sombra I, et al. Braz J Infect Dis 2021;25(S1):101045; Krentz HB, et al. AIDS Patient Care STDs 2022;36:1-10; IDWeek 2022. Poster 1252; Dou Y, et al. EACS 2021. Poster PE2/19; Gan X, et al. Curr HIV Res. 2022;20(3):222-7 ; Yang X, et al. Expert Rev Anti Infect Ther 2022, doi:10.1080/14787210.2022.2128766; Zhao F, et al. J Acquir Immune Defic Syndr. 2022; 91(S1): S42-50; Marcelin AG, et al. HIV Glasgow 2022. Poster P225; Noe S, et al. EACS 2019. Poster PE2/39; Beer D et al. HIV Glasgow 2022. Poster 177; Calza L, et al. J Antimicrob Chemother 2020;75:3327-33; ICAR 2016. Abstract P69; Foca E, et al. PLoS One. 2021;16:e0258533 ; Gianotti N, et al. IAS 2021. Poster PEB145; Gagliardini R, et al. CROI 2020. Poster 0486 ; Lanzafame M, et al. New Microbiol 2018;41:262-7; Malagnino V, et al. Microorganisms 2021;9:396; Int Assoc Provid AIDS Care 2022;21:23259582221101815; Dragoni F, et al. J Acquir Immune Defic Syndr. 2022 Dec 1;91(4):381-9; De Vito, A et al. HIV Glasgow 2022. Poster P085; Pagnucco L, et al. HIV Glasgow 2022. Poster P005; Pagnucco L, et al. HIV Glasgow 2022. Poster P198; Calza L, et al. J Acquir Immune Defic Syndr 2022;91:e9-e11; Vasyljev M, et al. HIV Glasgow 2022. Poster P080; Alves C and Carvalho AC. AIDS 2020. Poster PEB0235; Amor-García M, et al. Ann Pharmacother 2021;Aug 12:10600280211038504; Liano P, et al. PEB208; Hidalgo-Tenorio C, et al. Viruses 2022;14:504; Ferrero-Fernandez C, et al. EAHP 2020. Abstract 068; Mendez J, et al. Ann Pharmacother 2020;54:1424-7; Rodriguez-Villa A, et al. J Antimicrob Chemother 2017. Abstract P302; Tr...

Effectiveness outcomes reported in treatment-naïve patients who received DTG + 3TC in real-world studies

Reported effectiveness outcomes vary between unique cohorts (stated below chart)



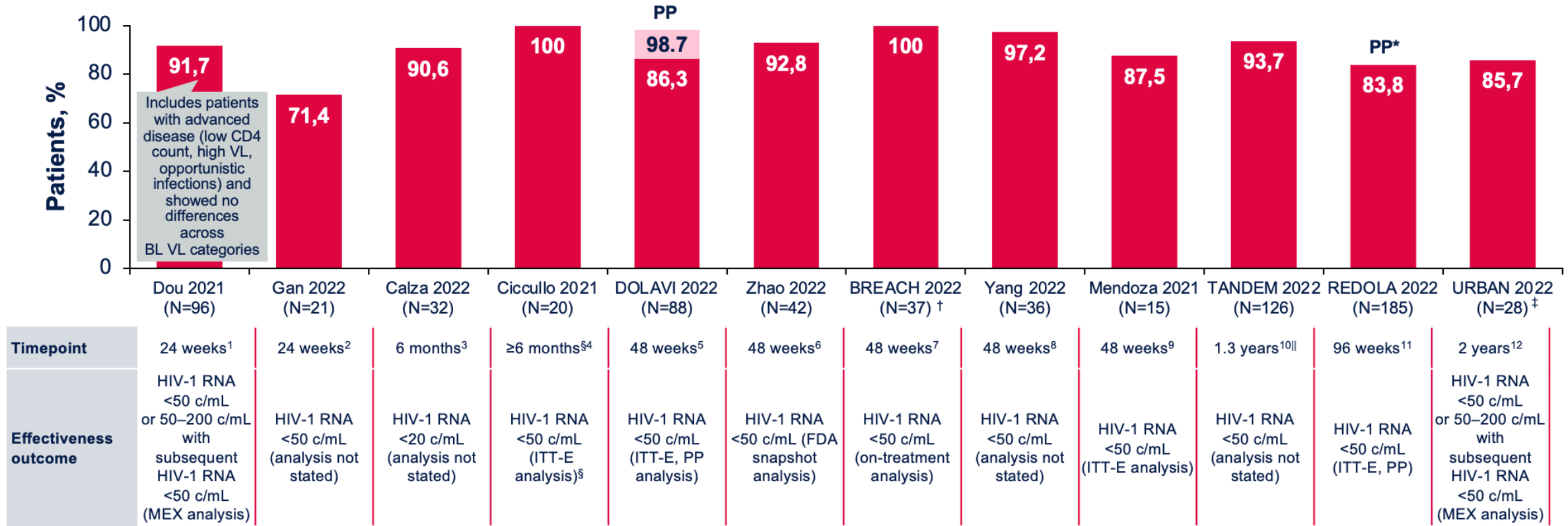
These data reinforce the high effectiveness of DTG/3TC in GEMINI-1 and -2 and STAT⁹⁻¹¹

Includes unique cohorts reporting applicable effectiveness outcomes for ≥10 treatment-naïve patients receiving DTG + 3TC; reported effectiveness outcomes vary between studies. Potential overlap between patient cohorts cannot be ruled out. *162 patients were included in the PP analysis; †Three patients were excluded from URBAN due to missing data; §Study reports "all patients achieved virologic suppression in the first 6 months from treatment initiation and maintained viral suppression during follow-up time with no viral blips registered" and "we did not observe any AE or treatment discontinuation", therefore this is considered an ITT-E analysis; ||Mean time over which treatment-naïve patients became suppressed was 14.1 weeks
 AE, adverse event; FDA, Food and Drug Administration; ITT-E, intention-to-treat exposed; MEX, missing equals excluded; PP, per protocol

1. Dou Y, et al. EACS 2021. Poster PE2/19; 2. Calza L, et al. J Acquir Immune Defic Syndr 2022;89:e30–2 [132] 3. Zhao F, et al. J Acquir Immune Defic Syndr, 2022; 91(S1): S16-S19 4. Yang X, et al. Expert Rev Anti Infect Ther 2022, doi:10.1080/14787210.2022.2128766 5. Mendoza I, et al. Ann Pharmacother. 2021;10600280211034176 6. Schneider S, et al. AIDS 2022. Poster EPB147 7. Pulido F, et al. HIV Glasgow 2022. Poster P059 8. Beer D et al. HIV Glasgow 2022. Poster 177 9. Cahn P, et al. Lancet 2019;393:143–55 10. Cahn P, et al. J Acquir Immune Defic Syndr 2020;83:310–8 11. Rolle CP, et al. AIDS 2021;35:1957–65

Effectiveness outcomes reported in treatment-naïve patients who received DTG + 3TC in real-world studies

Reported effectiveness outcomes vary between unique cohorts (stated below chart)

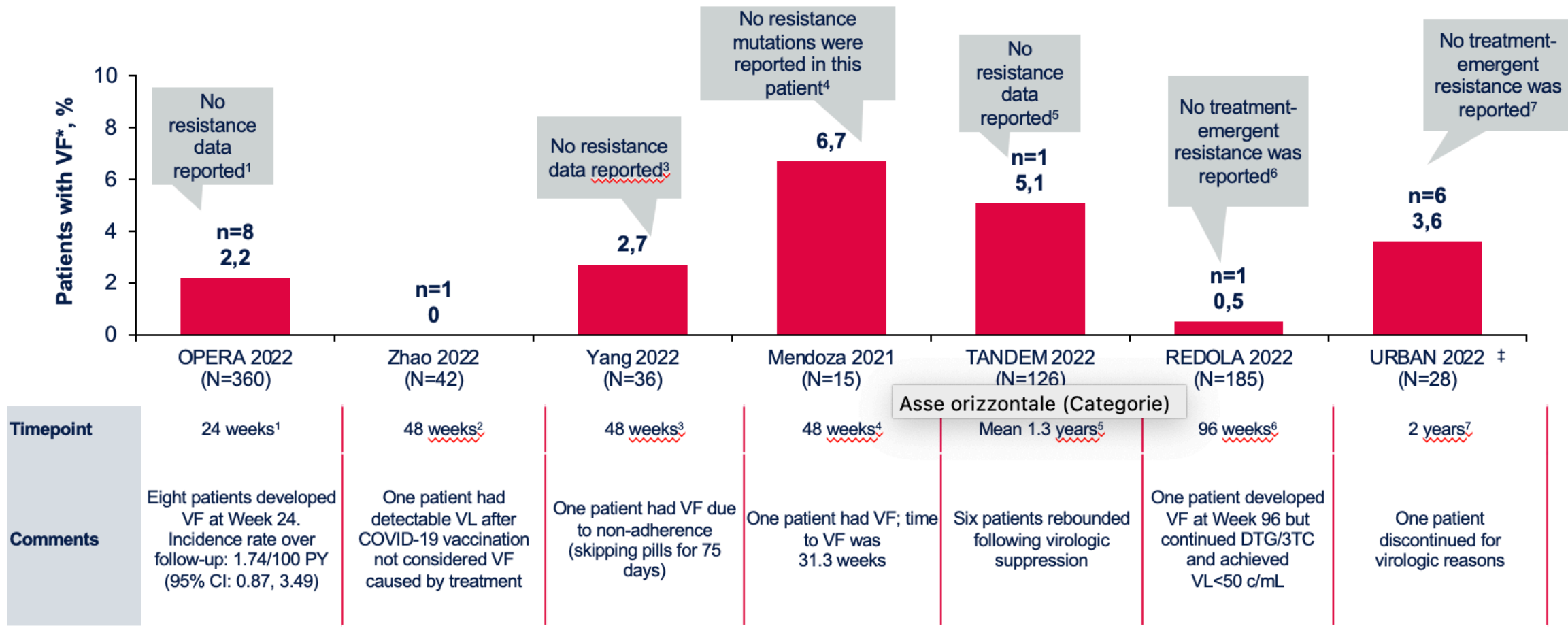


These data reinforce the high effectiveness of DTG/3TC in GEMINI-1 and -2 and STAT^{13–15}

Includes unique cohorts reporting applicable effectiveness outcomes for ≥10 treatment-naïve patients receiving DTG + 3TC; reported effectiveness outcomes vary between studies. Potential overlap between patient cohorts cannot be ruled out. *162 patients were included in the PP analysis; †N=37 treatment-naïve patients at BL; n at Week 48 not reported; ‡Three patients were excluded from URBAN due to missing data; §Study reports “all patients achieved virologic suppression in the first 6 months from treatment initiation and maintained viral suppression during follow-up time with no viral blips registered” and “we did not observe any AE or treatment discontinuation”, therefore this is considered an ITT-E analysis; ||Mean time over which treatment-naïve patients became suppressed was 14.1 weeks
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References: 1. Dou Y, et al. EACS 2021. Poster PE2/19 [44] 2. Gan X, et al. Curr HIV Res. 2022;20(3):222–7 [106] 3. Calza L, et al. J Acquir Immune Defic Syndr 2022;89:e30–2 [132] 4. Ciccullo A, et al. AIDS Res Hum Retroviruses 2021;37:486–8 [27b] 5. Hidalgo-Tenorio C, et al. Viruses 2022;14:524 [40b] 6. Zhao F, et al. J Acquir Immune Defic Syndr. 2022; 91(S1): S16–S19 [115] 7. Nasreddine R, et al. HIV Med 2022;doi: 10.1111/hiv.13373 (and Suppl. Appendix) [105b] 8. Yang X, et al. Expert Rev Anti Infect Ther 2022, doi:10.1080/14787210.2022.2128766 [114] 9. Mendoza I, et al. Ann Pharmacother. 2021;10600280211034176 [66] 10. Schneider S, et al. AIDS 2022. Poster EPB147 [108a] 11. Pulido F, et al. HIV Glasgow 2022. Poster P059 [20c] 12. Beer D et al. HIV Glasgow 2022. Poster 177 [87c] 13. Cahn P, et al. Lancet 2019;393:143–55 14. Cahn P, et al. J Acquir Immune Defic Syndr 2020;83:310–8 15. Rolle CP, et al. AIDS 2021;35:1957–65

Virologic failure and resistance in treatment-naïve patients treated with DTG + 3TC in real-world studies

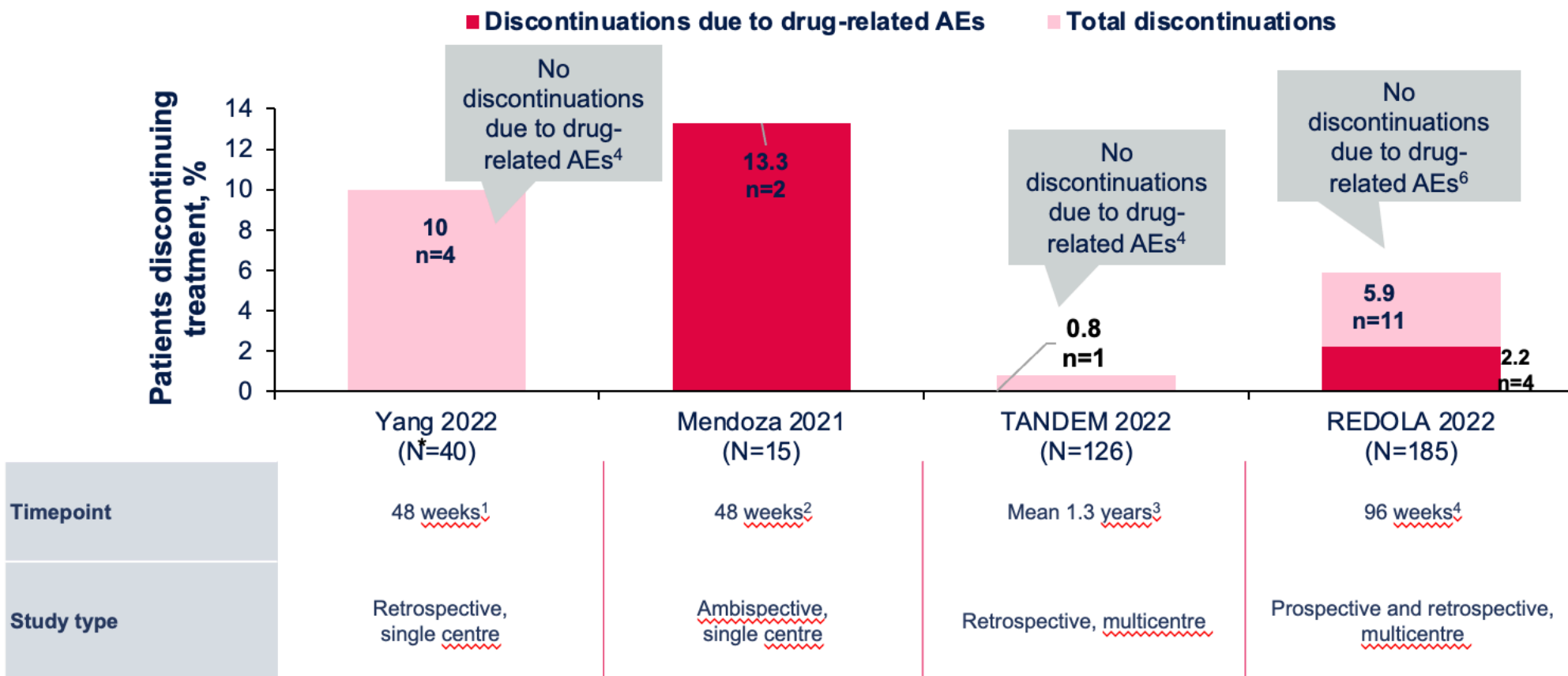


No treatment-emergent resistance has been reported in ART-naïve patients treated with DTG + 3TC in real life. These data reinforce the high barrier to resistance of DTG/3TC observed in GEMINI-1 and -2 and STAT⁸⁻¹⁰

Includes unique cohorts reporting VF outcomes for ≥10 treatment-naïve patients receiving DTG + 3TC; reported outcomes vary between studies. Potential overlap between patient cohorts cannot be ruled out; *Definitions of VF: REDOLA, two consecutive plasma HIV-1 RNA ≥50 c/mL; Mendoza, confirmed HIV-1 RNA >50 c/mL without documented suboptimal compliance; URBAN, investigator's discretion, TANDEM, Yang and Zhao, not specified; ‡Three patients excluded from URBAN due to missing data CI, confidence interval; PY, person-years; PYFU, person-years of follow-up

References: 1. Pierone G, et al. HIV Glasgow 2022; Poster 057 [119] 2. Zhao F, et al. J Acquir Immune Defic Syndr. 2022; 91(S1): S16-S19 [115] 3. Yang X, et al. Expert Rev Anti Infect Ther 2022, doi:10.1080/14787210.2022.2128766 [114] 4. Mendoza T, et al. Ann Pharmacother 2021;10600280211034176 [66] 5. Schneider S, et al. AIDS 2022. Poster EPB147 [108a] 6. Pulido F, et al. HIV Glasgow 2022. Poster P059 [20c] 7. Beer D et al. HIV Glasgow 2022. Poster 177 [87c] 8. Cahn P, et al. Lancet 2019;393:143-55 9. Cahn P, et al. J Acquir Immune Defic Syndr 2020;83:310-8 10. Rolle CP, et al. AIDS 2021;35:1957-65

Discontinuation due to drug-related adverse events in treatment-naïve patients who received DTG + 3TC in real-world studies



Discontinuation due to drug-related AEs appears to be low with DTG + 3TC in real-world studies, mirroring the rates seen in GEMINI-1 and -2 and STAT⁵⁻⁷

Data only included for unique cohorts with patients treated with DTG + 3TC that reported discontinuation for safety/tolerability reasons. Potential overlap between patient cohorts cannot be ruled out. Percentage calculated based on overall N for treatment-naïve patients who received DTG + 3TC. *23 patients excluded from overall N due to failing to achieve VL detection on time at clinic visits (mainly because of financial difficulties)

References: 1. Yang X, et al. Expert Rev Anti Infect Ther 2022, doi:10.1080/14787210.2022.2128766 [114] 2. Mendoza I, et al. Ann Pharmacother 2021;10600280211034176 [66] 3. Schneider S, et al. AIDS 2022. Poster EPB147 [108a] 4. Pulido F, et al. HIV Glasgow 2022. Poster P059 [20c 5. Cahn P, et al. Lancet 2019;393:143–55 6. Cahn P, et al. J Acquir Immune Defic Syndr 2020;83:310–8 7. Rolle CP, et al. AIDS 2021;35:1957–65

CARATTERISTICHE DELLA POPOLAZIONE NAÏVE IN TRATTAMENTO CON DTG/3TC

TN:63

Età all'arruolamento (media, \pm SD)	37.7 (\pm 9.69)
Sesso (N, %)	
M	51 (81%)
F	12 (19%)
Etnia (N, %)	
Caucasico	53 (84.1%)
Altro	10 (15.9%)
Fattore di rischio (N, %)	
Via sessuale	61 (96.8%)
IVDU	1 (1.6%)
Altro	1 (1.6%)
Stadio CDC (N, %)	
A	54 (85.7%)
B	6 (9.5%)
C	2 (3.2%)
No data	1 (1.6%)
HIV RNA al baseline (N, %)	
Undetectable	0 (0%)
Detectable	63 (100%)
CD4 al baseline (media, \pm SD)	557 (\pm 289)
CD4/CD8 al baseline (media, \pm SD)	0.71 (\pm 0.48)
Anni di TARV (mediana, IQR)	-
Mesi di follow up (mediana, IQR)	18 (9 – 34)

Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial



Paul E Sax, Anton Pozniak, M Luisa Montes, Ellen Koenig, Edwin DeJesus, Hans-Jürgen Stellbrink, Andrea Antinori, Kimberly Workowski, Jihad Slim, Jacques Reynes, Will Garner, Joseph Custodio, Kirsten White, Devi SenGupta, Andrew Cheng, Erin Quirk

-

Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial



Joel Gallant, Adriano Lazzarin, Anthony Mills, Chloe Orkin, Daniel Podzamczar, Pablo Tebas, Pierre-Marie Girard, Indira Brar, Eric S Daar, David Wohl, Jürgen Rockstroh, Xuelian Wei, Joseph Custodio, Kirsten White, Hal Martin, Andrew Cheng, Erin Quirk

Two randomized, double-blind, active-controlled studies

1,274 ART-naïve participants³

≥ 98% efficacy (M = E) after Week 48 at each study visit through Week 240³

0 cases of resistance to the components of B/F/TAF detected in the resistance analysis population³

BICSTaR Observational Cohort: 3-Yr Efficacy and Safety

- BICSTaR: prospective, multinational, observational cohort study of real-world safety and efficacy of BIC/FTC/TAF in treatment-naive and treatment-experienced people living with HIV
 - Main study: baseline to 2 yr (Yr 1-2)
 - Extension phase: participants in France, Germany, Canada given option to continue for 3 additional yr (Yr 3-5)
- Current report: 3-yr safety and efficacy of 435 participants who completed 36-mo visit by August 12, 2022 (completed main study and 1yr of extension)
 - Analysis population for main study: N = 781; n = 122 naive, n = 659 experienced
 - Entered extension phase: N = 449; n = 67 naive, n = 382 experienced

BICSTaR Observational Cohort: Virologic Efficacy at 3 Yr in People Who Were Treatment-Naive at BL

HIV-1 RNA <50 c/mL at 3 Yr, % (95% CI)	Treatment Naive at BL
Overall, by analysis	
▪ Missing = excluded (n = 60)	97 (89-100)
▪ Discontinuation = failure (n = 76)*	76 (65-85)
Late diagnosis (CD4+ cell count < 200 cells/mm ^{3†})	
▪ Yes (n = 11)	91 (59-100)
▪ No (n = 46)	98 (89-100)
Late diagnosis (CD4+ cell count < 350 cells/mm ^{3†})	
▪ Yes (n = 19)	95 (74-100)
▪ No (n = 38)	97 (85-100)
eGFR at BL ≥60 mL/min/1.73 m ² (n = 52)	96 (87-100)

*Reasons for discontinuation: adverse events, n = 8; death, n = 2; investigator decision, n = 1; participant decision, n = 3.

†And/or ≥1 AIDS-defining event.

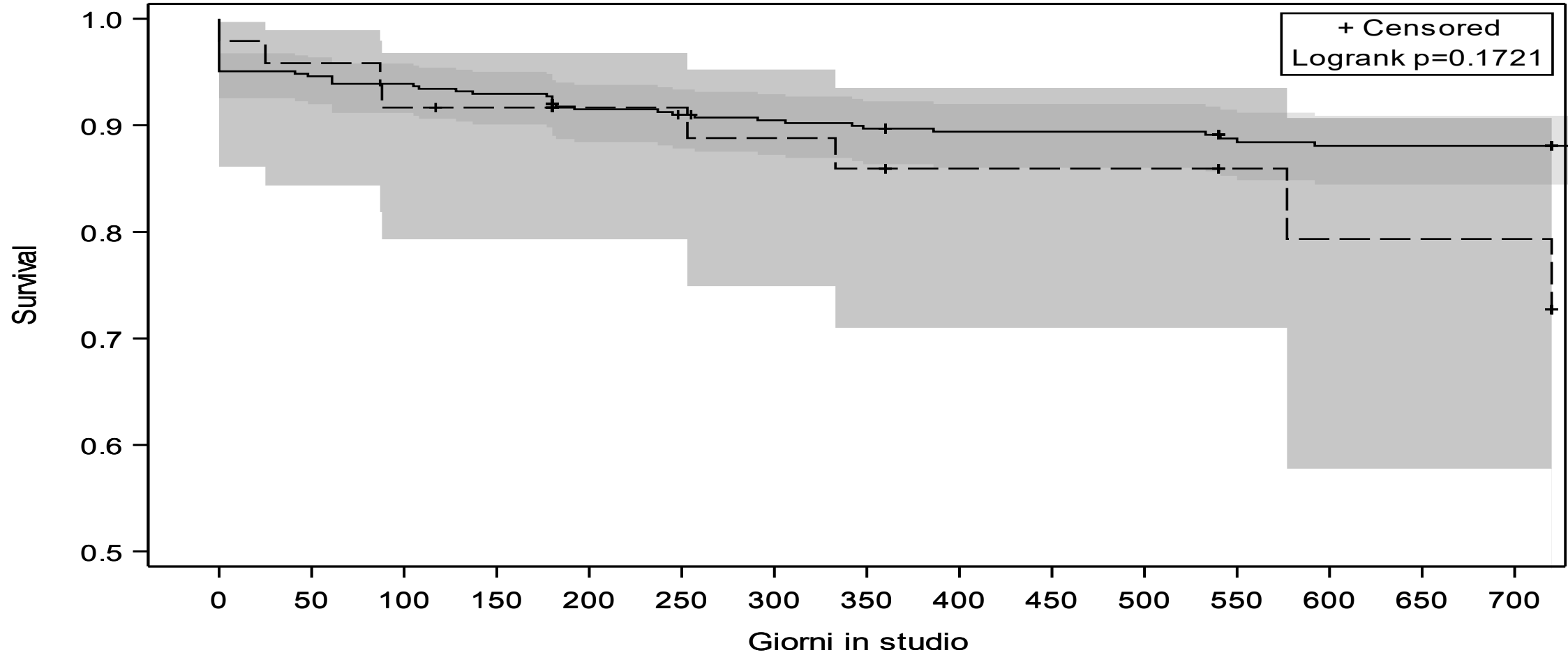
- Median change in CD4+ cell count at 3 yr (n = 52): +232 cells/mm³ (95% CI: +118 to +442)
- No reported emergence of resistance to components of BIC/FTC/TAF in treatment-naive or treatment-experienced group

BICSTaR Observational Cohort: Discontinuations of BIC/FTC/TAF Within 36 Mo

Discontinuations, n (%)	Total Population (N = 781)	Treatment Naive at BL (n = 122)	Treatment Exp'd at BL (n = 659)
Any reason	119 (15)	17 (14)	102 (16)
Adverse event	60 (8)	8 (7)	52 (8)
Participant decision	19 (2)	4 (3)	15 (2)
Investigator decision	16 (2)	2 (2)	14 (2)
Death	11 (1)	3 (2)	8 (1)
New treatment available	6 (1)	0	6 (1)
Lack of efficacy	5 (1)	0	5 (1)
Pregnancy	1 (<1)	0	1 (<1)
Missing	1 (<1)	0	1 (<1)

Caratteristiche della popolazione	PLWH, 475	TN, 48	TE, 427
Età media [anni]	49.2	38.1	50.4
Maschi, n (%)	319 (67)	32 (66)	287 (67)
Altezza [cm]	170.3	169.2	170.4
Familiarità cardiovascolare n (%)	83 (17)	10 (21)	73 (17)
Fumo n (%)	236 (50)	21 (44)	215 (50)
HbsAg positivo n (%)	21 (4)	0	21 (5)
HCVAb pos n (%)	122 (26)	1 (2)	121 (28)
HCV RNA pos n (%)	11 (2)	0	11 (2.5)
Lipodistrofia n (%)	64 (13)	1 (2)	63 (15)
CDC stadio C n (%)	50 (10)	6 (12)	44 (10)
CD4+ nadir, N/mmc	257.5	339.9	247.1
HIV-RNA zenit, copies/mm ³	445516.1	939197.2	383806
Anni dalla diagnosi di HIV	14.1	0	15.7
Anni di terapia antiretrovirale	11.3	0	12.7

Product-Limit Survival Estimates
 Con numero di soggetti a rischio e limiti di confidenza al 95%



Naive ——— N - - - S

N	426	403	400	396	355	352	349	346	308	308	308	255	253	253	253
S	48	46	44	43	32	32	31	30	21	21	21	13	12	12	12

LA TERAPIA ART

- Ragionata
- Efficace
- Non deve fallire
-Come negli scacchi lasciarti aperte le mosse future

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