PANDORA ID-25
Ospedale San Paolo - 8 settembre 2025

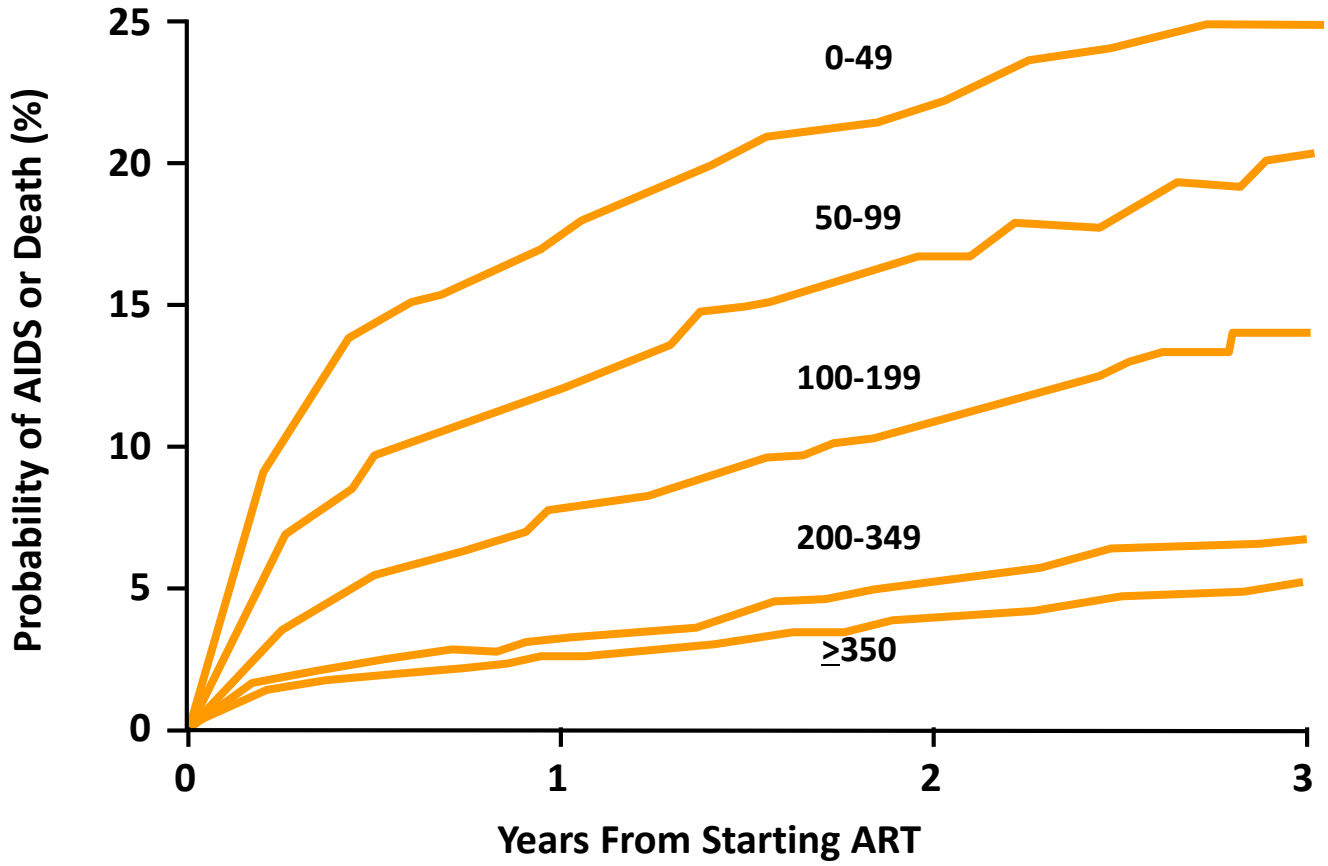
La terapia antiretrovirale oggi nei LP – Quale spazio per la terapia a 3 farmaci

Stefano Rusconi
DIBIC - UNIMI
S.C. Malattie Infettive
ASST Ovest Milanese, Legnano (Mi)

COIs

ViiV Healthcare, Gilead Sciences, MSD, Menarini, AstraZeneca

Prognosis from starting ART according to pre-therapy CD4 cell counts (cells/µL)



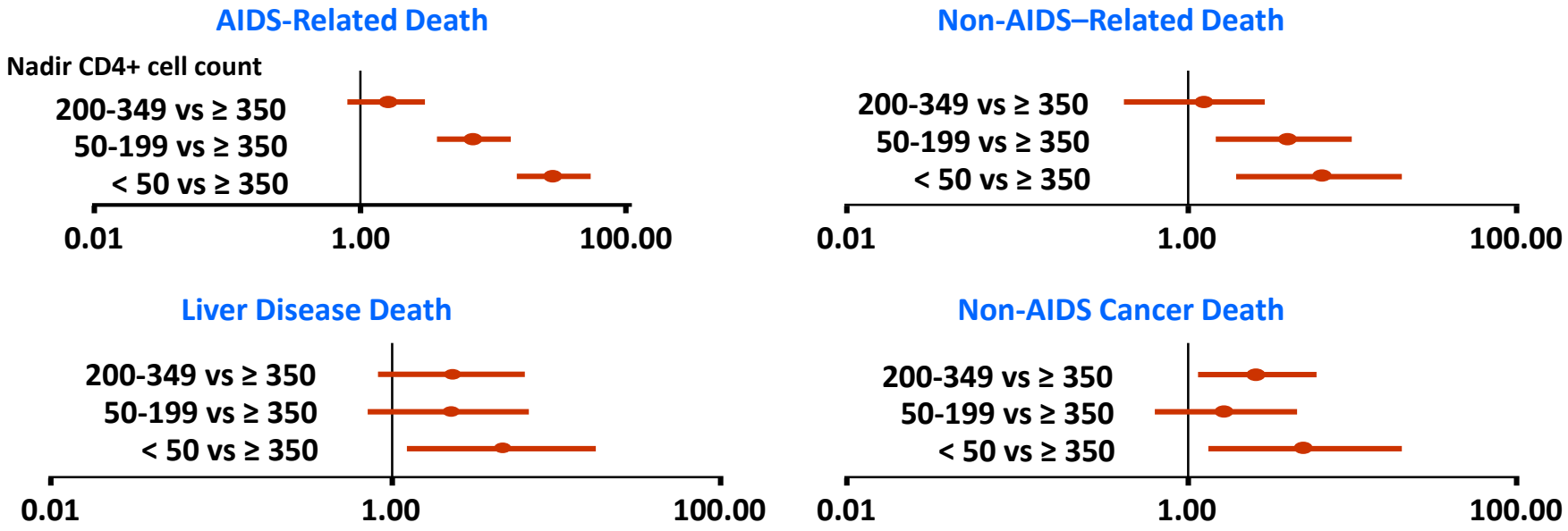
HIV in Europe

ART CC. Egger et al, Lancet. 2002

CASCADE:

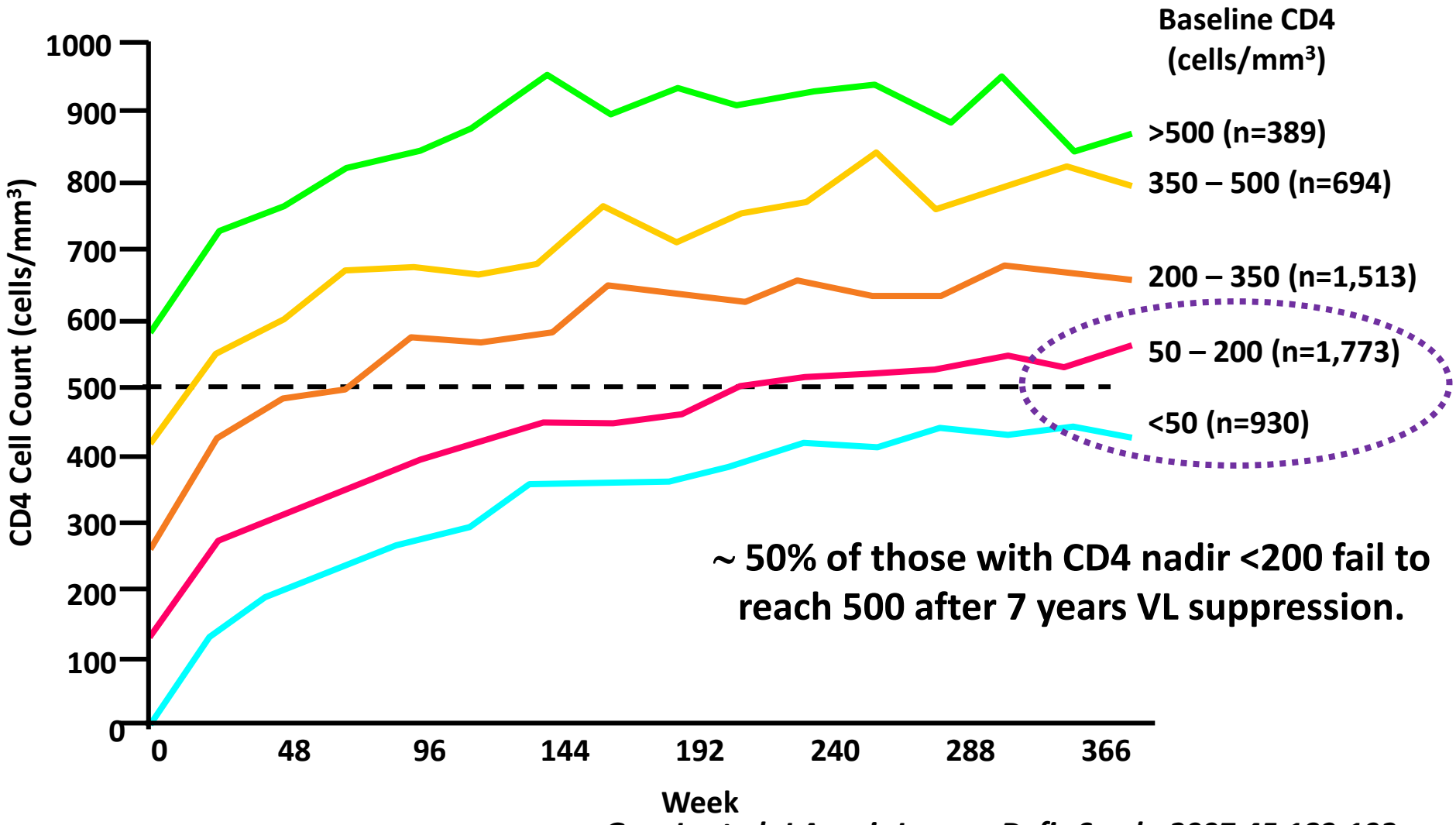
Nadir CD4+ Cell Count Predicts AIDS and Non-AIDS Events

- CASCADE Collaboration cohort: N = 9858
- Several clinical markers of HIV progression correlated with death due to AIDS-related causes, non-AIDS–related severe infection, liver diseases, and non-AIDS–related malignancies including
  - Latest and nadir CD4+ cell counts
  - Time spent with CD4+ cell count < 350 cells/mm^3



Marin B, et al. IAS 2007. Abstract WEPEB019.

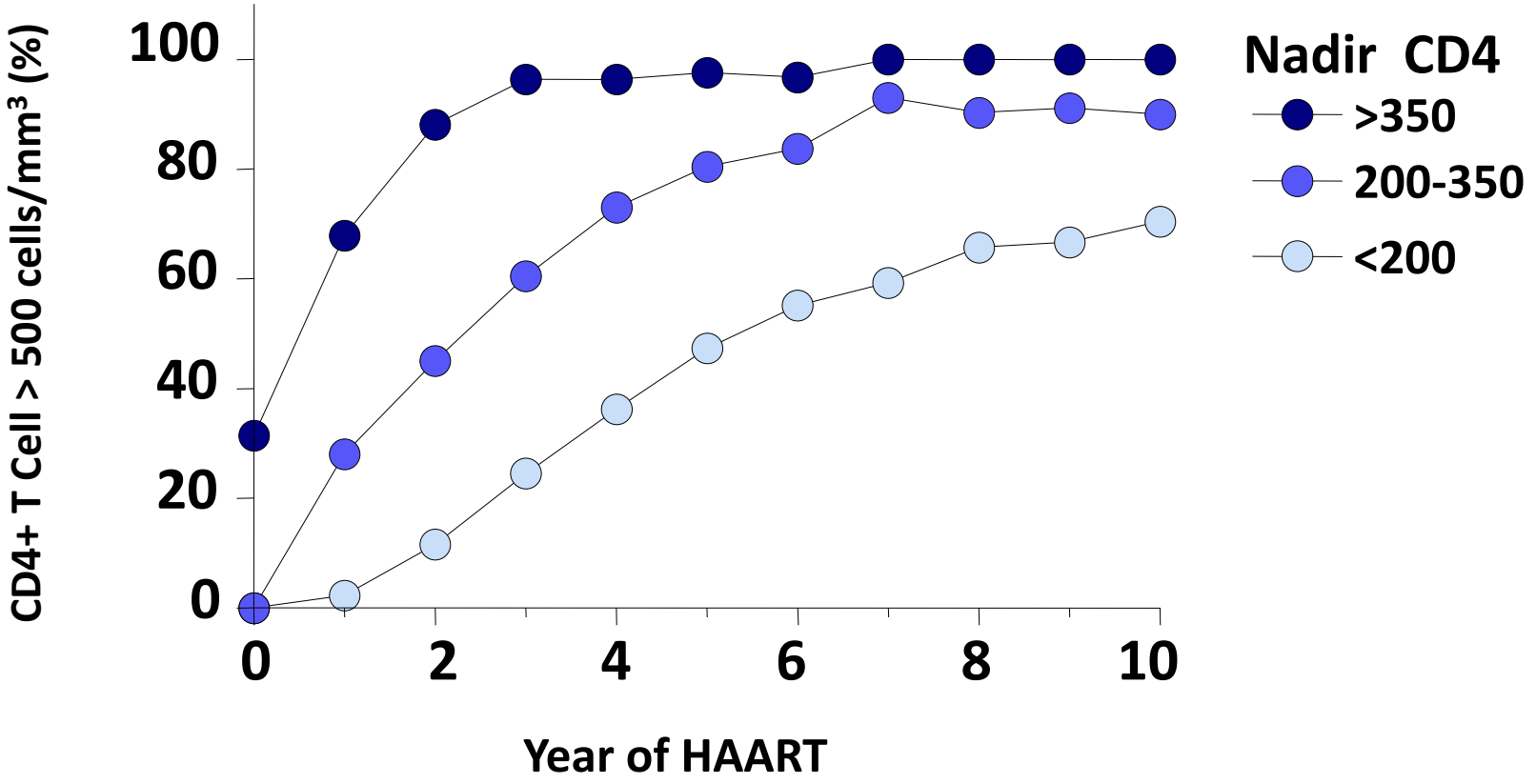
Suboptimal CD4 T Cell Gains Are Common Among Patients Who Initiate HAART Late (ATHENA)



~ 50% of those with CD4 nadir <200 fail to reach 500 after 7 years VL suppression.

Gras L, et al. J Acquir Immun Defic Syndr. 2007;45:183-192.

CNICS: ~ 40% of patients with a nadir CD4 < 200 fail to achieve a normal CD4+ cell count, even after 10 years of viral suppression (n=300)



Kelley CF, et al. Clin Infect Dis 2009;48:787-794.

The Impact of Late Diagnosis on Health Outcomes

Individual

- 17-fold higher risk of death over the first year
- An extended period of uncontrolled viraemia
  - with immune inflammation and activation
- Higher incidence rates
  - for AIDS Defining Events Serious Non-AIDS Events , including heart,liver, and kidney-related disease and some cancers and deaths

HIV Med. 2022;23:1118–1126.

The Impact of Late Diagnosis on Health Outcomes

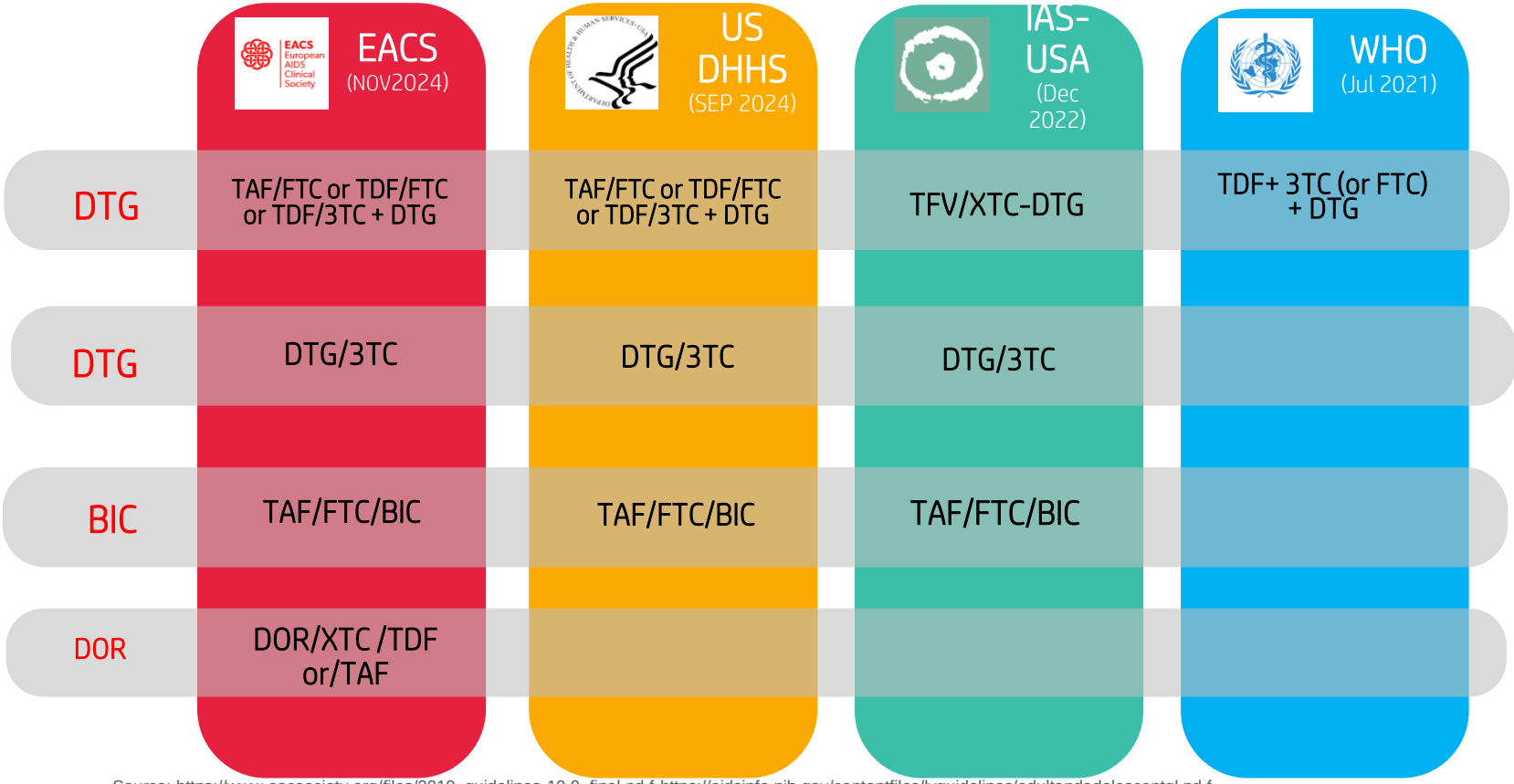
Population level

- Late diagnosis, now estimated to be a median of 3–5 years after infection,
  - increases the risk of further HIV transmission as viral load steadily increases

HIV Med. 2022;23:1118–1126.

International Guidelines-Preferred Combinations

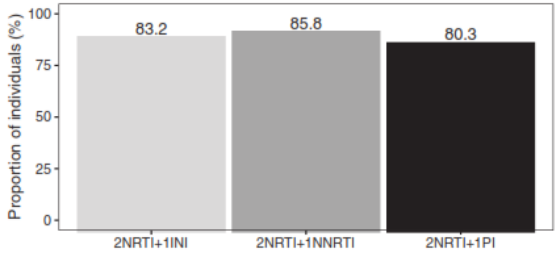
No clear Guidance for Late Presenters

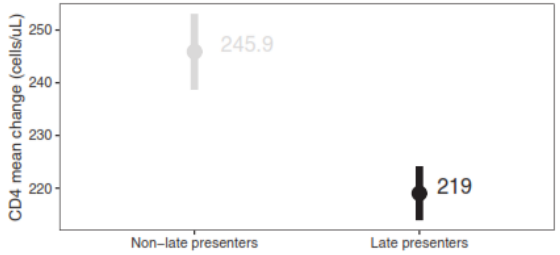


Source: https://www.eacsociety.org/files/2019_guidelines-10.0_final.pd.f https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pd.f
https://www.iasusa.org/wp-content/uploads/guidelines/arv/arv_2018.pdf https://apps.who.int/iris/bitstream/handle/10665/325892/WHO-CDS-HIV-19.15-eng.pdf?ua=1

There are cohort data to guide us

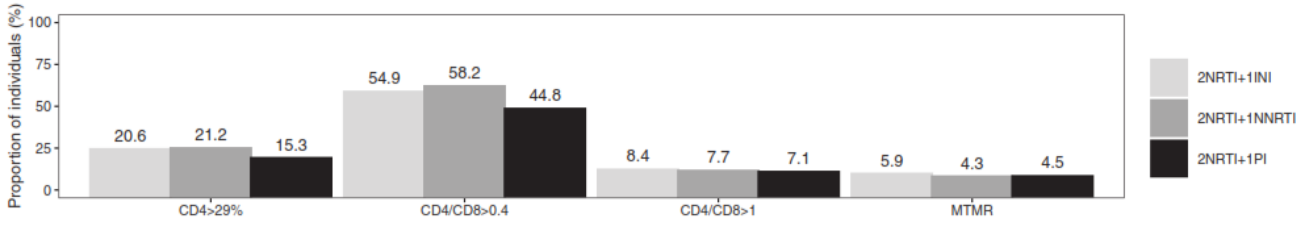
Viral suppression and immunological response in late presenters by initial ART regimen





Viral suppression	NNRTI	PI
N	3900	
Unadj OR	1.22 (0.89, 1.67)	0.82 (0.62, 1.08)
Adj OR	1.36 (1.00, 1.85)	1.03 (0.75, 1.43)

Mean change (95% CI) in CD4 count	NNRTI	PI
N	3900	
Unadj OR	−30.81 (−45.21, −16.42)	−20.25 (−37.52, −2.97)
Adj OR	−6.45 (−22.23, 9.32)	8.76 (−9.38, 26.90)



OR* (95% CI) ref: INI−based

	CD4>29%: NNRTI	CD4>29%: PI	CD4/CD8>0.4: NNRTI	CD4/CD8>0.4: PI	CD4/CD8>1: NNRTI	CD4/CD8>1: PI	MTMR: NNRTI	MTMR: PI
N	3230		2637		2637		2130	
Unadj OR	1.04 (0.80, 1.34)	0.70 (0.57, 0.85)	1.14 (0.88, 1.48)	0.66 (0.54, 0.82)	0.92 (0.62, 1.36)	0.83 (0.56, 1.23)	0.71 (0.46, 1.11)	0.75 (0.45, 1.23)
Adj OR	1.01 (0.79, 1.30)	1.02 (0.83, 1.26)	0.95 (0.71, 1.28)	0.92 (0.72, 1.18)	0.80 (0.49, 1.30)	1.19 (0.72, 1.96)	0.70 (0.42, 1.16)	1.31 (0.76, 2.26)

AIDS 2021, Vol 35 No 8

MTMR multiple T-cell marker recovery

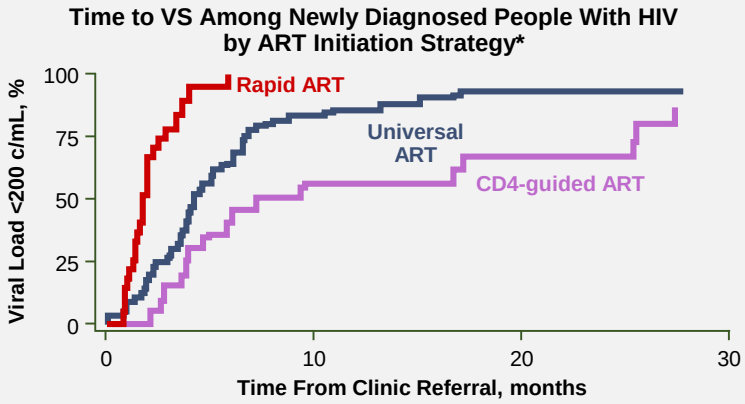
NNRTI and INSTI Rx better than bPI

But… do Late Presenters need Rapid Start?

From the LP data it seems they are a priority

Rapid Start-Time to virologic suppression and impact on reservoir may benefit Late presenters

Time to VS with rapid ART versus universal ART[2,*]



ART initiated within ≤30 days of HIV acquisition led to **faster and more sustained decay of HIV reservoir markers** than ART initiated within 31–90 days or >24 weeks after acquisition[4,¶]

*A US clinic-based cohort study in people with new HIV diagnosis. Rapid (2013–2014; n=39) ART initiation as soon as possible, preferably on the day of diagnosis; Universal (2010–2013; n=69): ART offered immediately to all people with HIV by primary care providers; CD4-guided (2006–2009; n=25): ART recommended if CD4 count <500 cells/mm;[3]
†P<0.0001 for rapid ART versus universal ART and CD4-guided ART; ¶Clinical record review in a UK cohort (July 2016–June 2018). Median 6 days from diagnosis to ART start among whole population (N=153); ‡Longitudinal analysis of data (Oct. 2014–Nov. 2018) from MERLIN study in Peru (N=56). VS, virologic suppression

1. DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed July 19, 2024); 2. Pilcher CD, et al. J *Acquir Immune Defic Syndr*. 2017;74:44-51;
3. Girometti N, et al. *HIV Med.* 2020;21:613-5; 4. Massanella M, et al. *Lancet Microbe.* 2021;2:e198-209

Start ART at diagnosis (when possible) to increase uptake, decrease time to linkage & virologic suppression, & to improve the rate of virologic suppression

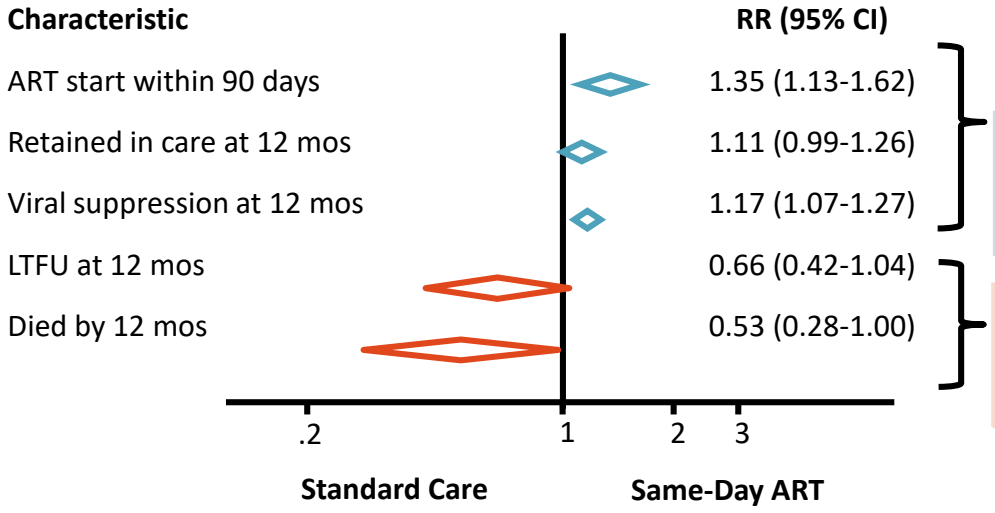
Offer same day ART:
Primary HIV infection
Patient wishes to do so
LTFU more likely if not started

IAS–USA
International Antiviral Society–USA
2023

Soon as possible after diagnosis,
ideally within 7 days, including on the same day as diagnosis or at the first clinic visit
if the patient is ready and there is
no suspicion for a concurrent opportunistic infection

Improved Clinical Outcomes With Rapid ART Initiation

- **Systematic review of rapid ART initiation (including 4 RCTs)**



Same-day ART associated with:

- **Increased** likelihood of ART initiation, retention in care, viral suppression
- **Decreased** likelihood of loss to follow-up and death

1. Ford. AIDS. 2018;32:17.

What do the Guidelines Say?

Recommendations for Same-Day ART Initiation

Drugs to Use in Rapid Start are not currently the same as the guidance for Naïve patients

bPI not in naïve start, but in some Rapid Start guidance

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

Bictegravir/TAF/FTC
Dolutegravir + TAF or TDF + XTC
Darunavir/b + TAF or TDF + XTC
AVOID NNRTI, DTG/3TC & ABC

EACS European AIDS Clinical Society
2021

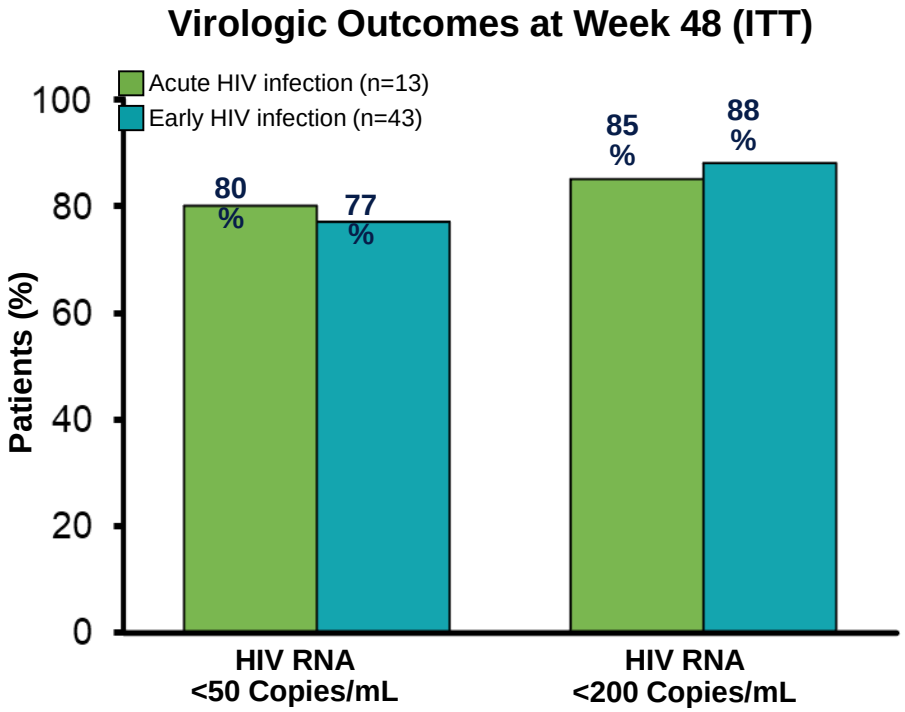
Dolutegravir+TDF or TAF + FTC
Bictegravir/TAF/FTC
DRV/b + TAF or TDF + XTC

IAS–USA
International Antiviral Society–USA
2023

Bictegravir/TAF/FTC
Dolutegravir + TAF or TDF + XTC

DIAMOND Study
Rapid ART in Patients with Acute and Early HIV Infection treated with Darunavir/c/F/TAF

- HIV RNA <50 copies/mL at week 48
  - ITT analysis: 84%
  - Observed analysis: 96%
  - Similar rates in both subgroups
- No discontinuations due to lack of efficacy or baseline resistance
- Discontinuations due to:
  - Adverse events (n=1, early HIV infection: allergic dermatitis/pyrexia/lip swelling, resolved after stopping drug)
- Results indicate that rapid initiation of darunavir/c/F/TAF achieved high rates of virologic suppression in patients with acute and early HIV infection
- **21% had CD4+ cell count <200 cells/µL**



Dunn K, et al. *Clin Infect Dis 2020 Dec 15;71(12):3110-3117.*

Efficacy and Safety Profile of B/F/TAF in a Rapid Start Model

FAST: National, prospective, single-arm multicentre study (France)

N = 112 (ITT)

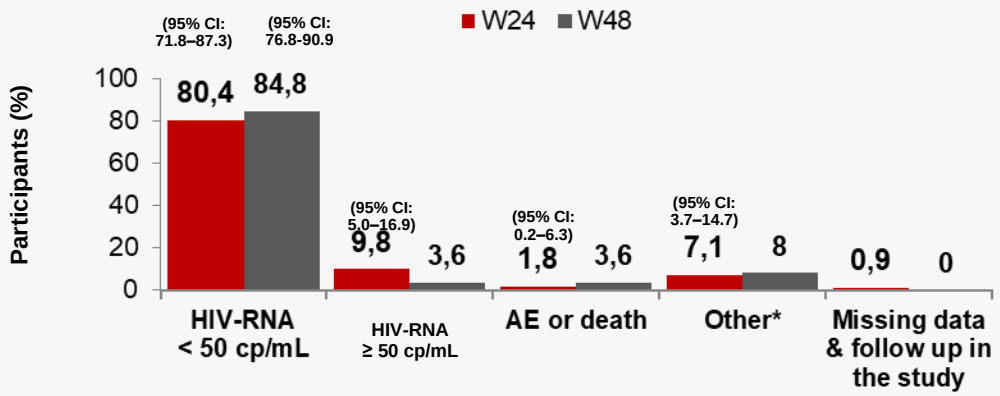
People with HIV initiating B/F/TAF before any laboratory results were available (rapid start)

Baseline Characteristics

Baseline characteristics, median (IQR) or n (%)	ITT (n = 112)
Age, median (range), years	36 (28–47)
Male	98 (87.5)
HIV RNA, log_{10} cp/mL HIV RNA > 100,000 cp/mL HIV RNA > 500,000 cp/mL Primary infection	4.8 (4.4–5.5) 50 (44.6) 21 (18.8) 23 (19.6)
CD4 count, cells/mm³ **CD4 < 200 cells/mm3**	**369 (240–570)** **19 (17.2)**
Time to enrolment since first HIV diagnosis, median (range), days	8 (5–17)
Positive HBsAg	2 (1.8)
Time between inclusion and initiation of treatment, days 0 1	 110 (98 2 (1.8

Virologic Outcomes at Week 24 & 48

ITT FDA Snapshot



No emergent RAMs were detected in people with HIV who failed to achieve HIV-1 RNA < 50 cp/mL

B/F/TAF was well tolerated and effective for same-day ART initiation in a rapid start setting

Other: Baseline RAMs according to the 2019 French HIV resistance algorithm (n=3, 2.7%): one had a pre-therapeutic M184V mutation resistance, two had E157Q polymorphism in the integrase gene. Lost to follow-up (n=3, 2.7%); relocation (n=2, 1.8%), incarceration (n=1, 0.9%)
HBsAg, hepatitis B surface antigen; ITT, intent-to-treat; VL, viral load

1. Adapted from Bachelard A, et al. EACS 2021, Poster PE2/7; 2. Bachelard A, et al. 23rd French National Infectious Disease day (June 2022)

Efficacy and Safety Profile of Rapid Start of B/F/TAF in Late Presenters

RAINBOW: Phase 4, single-centre, single-arm study (Italy)

N = 30

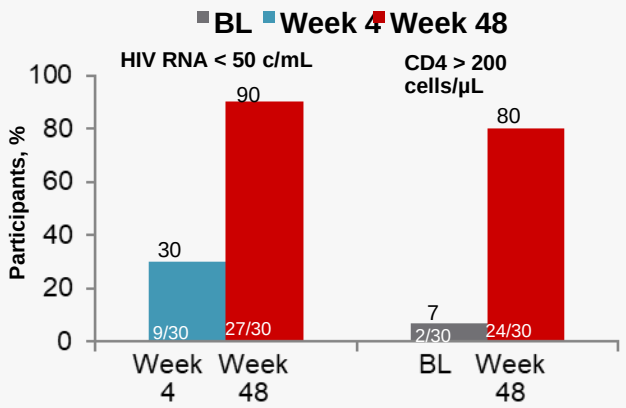
ART-naïve participants presenting at HIV-1 diagnosis with advanced disease*

Outcomes

Efficacy, safety profile and feasibility of rapid ART initiation strategy†

Baseline Characteristic	N = 30
CD4 cell count, cell/mm^3, median (IQR)	90 (39–147)
HIV RNA at BL, log$_{10}$ c/mL, median (IQR)	6.0 (5.4–6.4)

Results



- **No ART modification** was performed once GRT was reviewed
- **2 virologic failures at Week 48, both resuppressed** on B/F/TAF

- **No ART discontinuation** due to toxicity or virologic failure
- **6** SAEs (n = 3)
- **1** participant changed ART due to disseminated TB

- **Improvement** in total cognitive performance‡

Rapid start of B/F/TAF demonstrated high rates of virologic suppression and was generally well tolerated in people with advanced HIV

*Presence of an AIDS-defining event and/or CD4 cell count < 200 cells/µL; †B/F/TAF started within 7 days of HIV diagnosis; ‡Significant improvement (P < 0.05) for memory, fine motor functioning, working memory and neuropsychological performance (NPZ 12) domains.

BL, baseline; GRT, genotype resistance test; IQR, interquartile range; NPZ 12, neuropsychological test composite z score; TB, tuberculosis

Camici M, et al. AIDS 2022, Poster EPB151

B/F/TAF Rapid Initiation for Late-Presenting PWH

Retrospective cohort analysis (China)[1]
Single-center, retrospective, real-world EVIDENCE study (China)[2]

EVIDENCE: Week 24 and 48 Results[2]

N=54

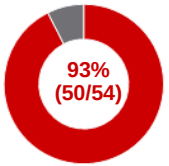
ART-naïve PWH with CD4 <200 cells/mL and/or with AIDS-defining illnesses who initiated B/F/TAF within 7 days of diagnosis

June 2021–October 2023

Outcomes: Efficacy and safety B/F/TAF rapid start (within 7 days) in people with advanced HIV

Baseline characteristics: Median age 42 years; 85% male sex; HIV-1 RNA, 5.18 log10 c/mL; median CD4 count, 121.5 cells/μL; 33% of cases complicated by opportunistic infections; median 4 days to ART initiation

VS at Week 48: HIV RNA <50 c/mL



4 participants not achieving VS all had HIV-1 RNA <100 c/mL

Safety

- There were no treatment discontinuations due to AEs
- No IRIS AEs were reported

CD4 count increased by 119 cells/μL from BL to Week 24 **(*P*<0.01)**

CD4:CD8 ratio increased by 0.12 **(*P*<0.01)**

B/F/TAF showed high rates of virologic suppression and was generally well tolerated in PWH with advanced disease, including as a rapid start treatment within 7 days of diagnosis[1,2]

BL, baseline; IRIS, immune reconstitution inflammatory syndrome; TRAE, treatment-related adverse event; VS, virologic suppression
[a]IRIS results were not reported in the poster
1. Long H, et al. HIV Glasgow 2024, Poster 087. 2. Zhu Y-C, et al. HIV Glasgow 2024, Poster 156

We now have Randomised Data in Late Presenters

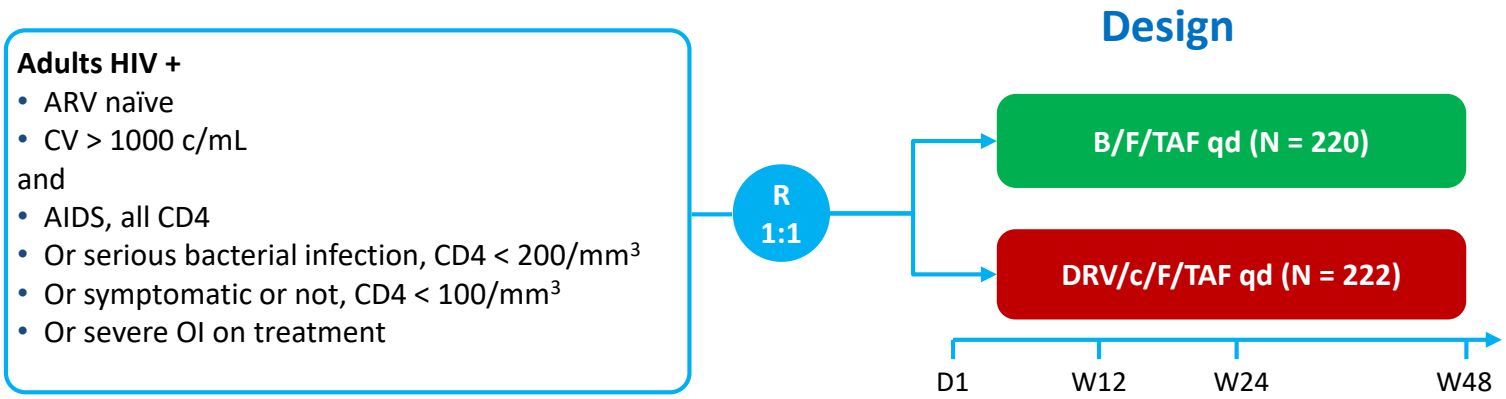
Most first line HIV treatment randomised controlled trials recruit individuals who have

- low baseline viral loads,
- high CD4 counts,
- fewer co-morbidities, drug-drug interactions, and other treatment failure risks

These clinical trials have been underpowered to assess the preferred antiretrovirals in therapy-naïve people with advanced HIV disease (PWAH).

LAPTOP: B/F/TAF vs D/c/F/TAF for first-line ART in PWH and advanced HIV

- Phase 4, randomized, **non-inferiority**, multicentric (7 European countries), consortium Neat-ID



- Composite primary endpoint: time to
  - Virologic failure (VL decrease < 1 $\log_{10}$ c/mL at W12 or > 50 c/mL at W48)
  - Or clinical failure

- Evaluation by Kaplan-Meier and Cox regression, non-inferiority margin = HR 1.606

Behrens G, CROI 2025, Abs. 658

Baseline characteristics

		Total (N=442)
Age (years), median (IQR)		43 (35-53)
Gender	Male	358 (81.0)
	Female	84 (19.0)
Ethnicity	White	276 (62.4)
	Black	83 (18.8)
	Other	83 (18.8)
CD4+ count <100 cells/µL		379 (85.8)
HIV RNA viral load >500,000 log10 copies/mL		197 (44.6)

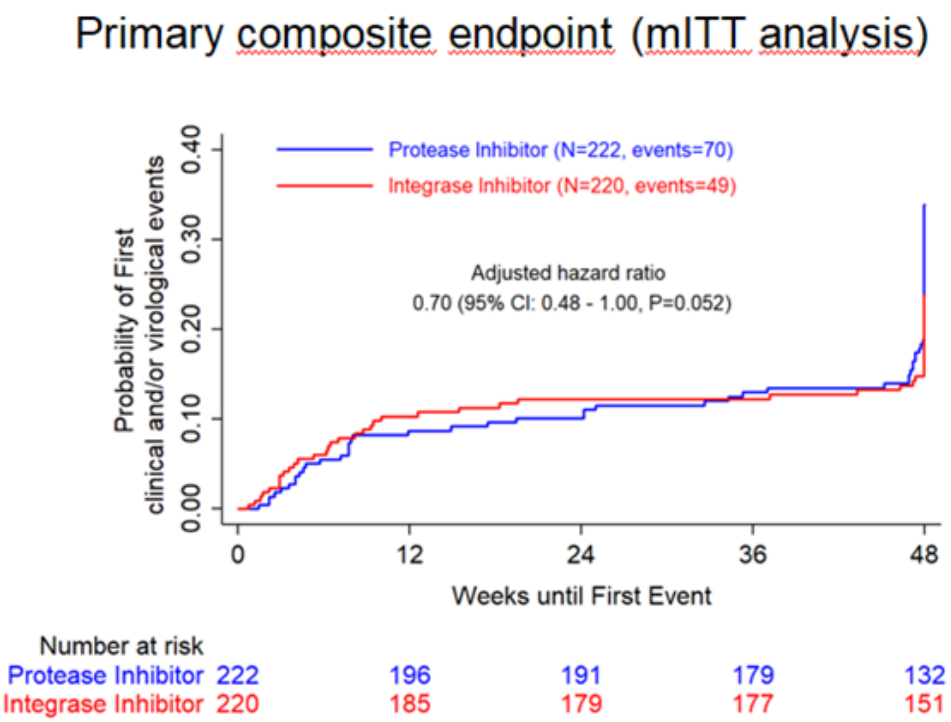
CROI 2025 P 0658

Primary Outcome

- Time to failure
  - as the first occurrence of any of a composite of
    - Insufficient virologic response
      - HIV-1 RNA reduction <1 log 10 copies/mL at week 12,
    - or viral load >50 HIV-1 RNA copies/mL at week 48
    - or clinical events

CROI 2025 P 0658

LAPTOP-Kaplan Meier curves for primary outcome



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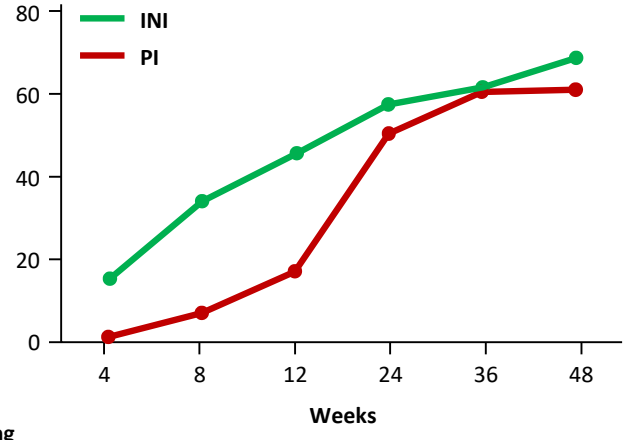
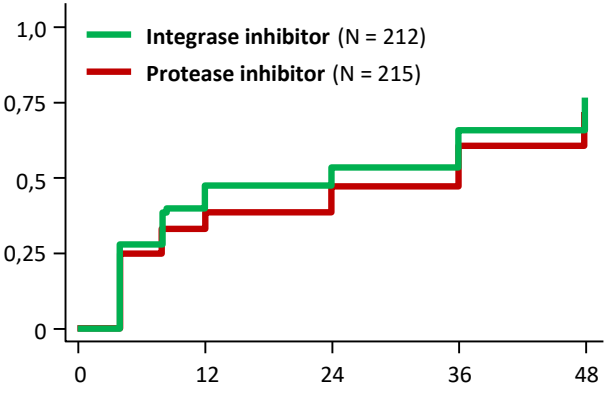
LAPTOP: B/F/TAF vs D/c/F/TAF for first-line ART in PWH and advanced HIV

VL < 50 cp/mL (%)



Missing (discontinuation/ missing in window)	4	8	12	24	36	48
INI	18	30	31	36	43	45
PI	11	21	20	27	33	38

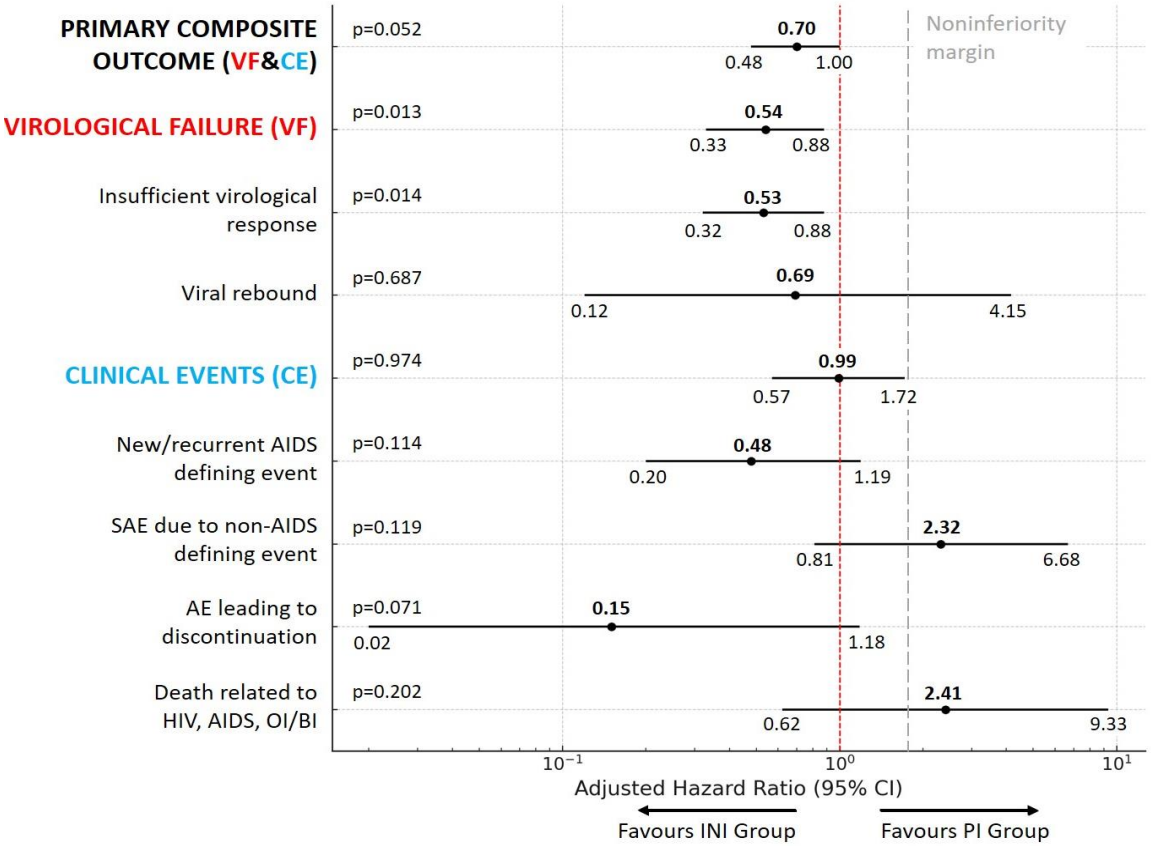
Time to CD4 > 200/mm^3 in participants with Baseline CD4 ≤ 200/mm^3 (Kaplan-Meier)



N at risk	0	12	24	36	48
Integrase inhibitor	215	132	119	100	52
Protease inhibitor	212	117	101	86	43

Behrens G, CROI 2025, Abs. 658

Results



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LAPTOP: B/F/TAF vs D/c/F/TAF for first-line ART in PWH and advanced HIV

Participants characteristics
N = 442

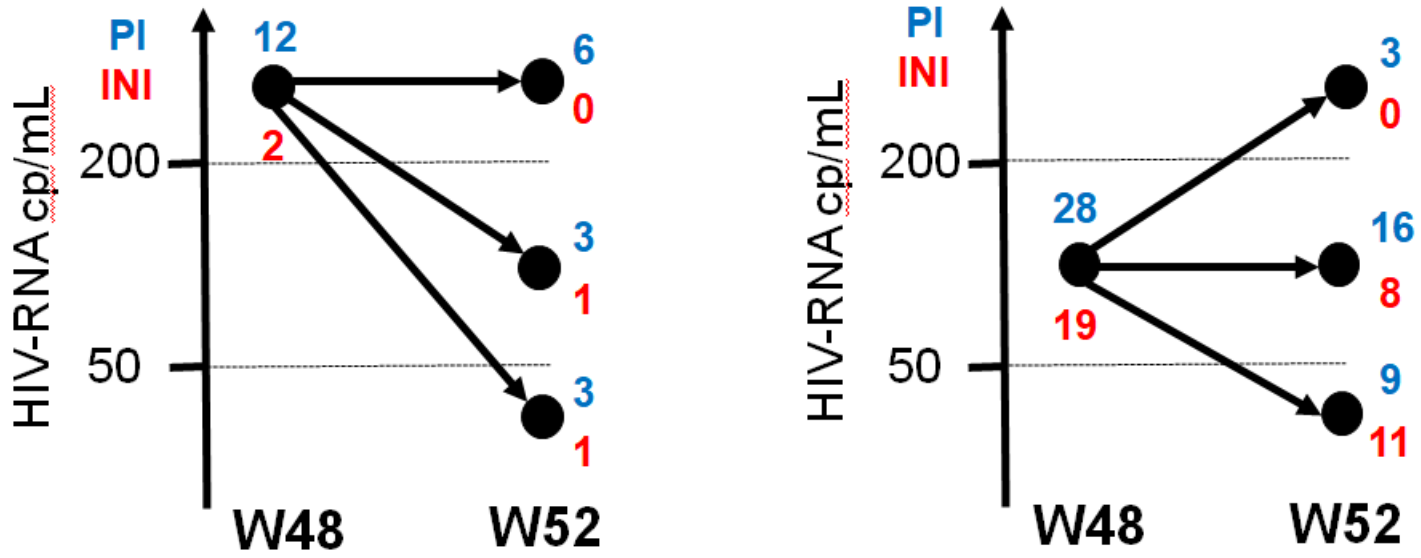
Characteristics	
Median age, years	43
Male, %	81.0 %
Ethnicity %: white/black	62.4 % / 18.8 %
Median (IQR) CD4/mm^3	41 (17 – 79)
CD4 < 100/mm^3	85.8 %
Median (IQR) VL, $\log_{10}$ c/mL	5.6 (5.1 -6.1)
VL > 500 000 c/mL	44.6 %

Primary endpoint and components (ITTm)

	B/F/TAF N = 220	D/c/F/TAF N = 222	aHR	p
Primary endpoint (V and/or C)	**49 (23.8 %)**	**70 (33.9 %)**	**0.70 (0.48-1.00)**	**0.052**
Virologic failure	25 (13.4 %)	46 (23.9 %)	0.54 (0.33-0.88)	0.013
Insufficient response	23 (12.4 %)	43 (22.5 %)	0.53 (0.32-0.88)	0.014
Virologic rebound	2 (1.0 %)	3 (1.5 %)	0.69 (0.12-4.15)	0.687
Clinical event	25 (11.8 %)	26 (12.1 %)	0.99 (0.57-1.72)	0.974
AIDS event > 28 days after ART start	7 (3.5 %)	15 (7.2 %)	0.48 (0.20-1.19)	0.114
Non-AIDS severe AE	11 (5.3 %)	5 (2.3 %)	2.32 (0.81-6.68)	0.119
AE leading to discontinuation	1 (0.5 %)	7 (3.3 %)	0.15 (0.02-1.18)	0.071
Death due to HIV-AIDS	7 (3.3 %)	3 (1.4 %)	2.41 (0.62-9.33)	0.202

Behrens G, CROI 2025, Abs. 658

Evolution of HIV-RNA in individuals with viral load >50 cp/mL at week 48



Participants with missing results/visits at week 52 or ART switch at week 48 were excluded from this analysis

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LAPTOP: B/F/TAF vs D/c/F/TAF for first-line ART in PWH and advanced HIV

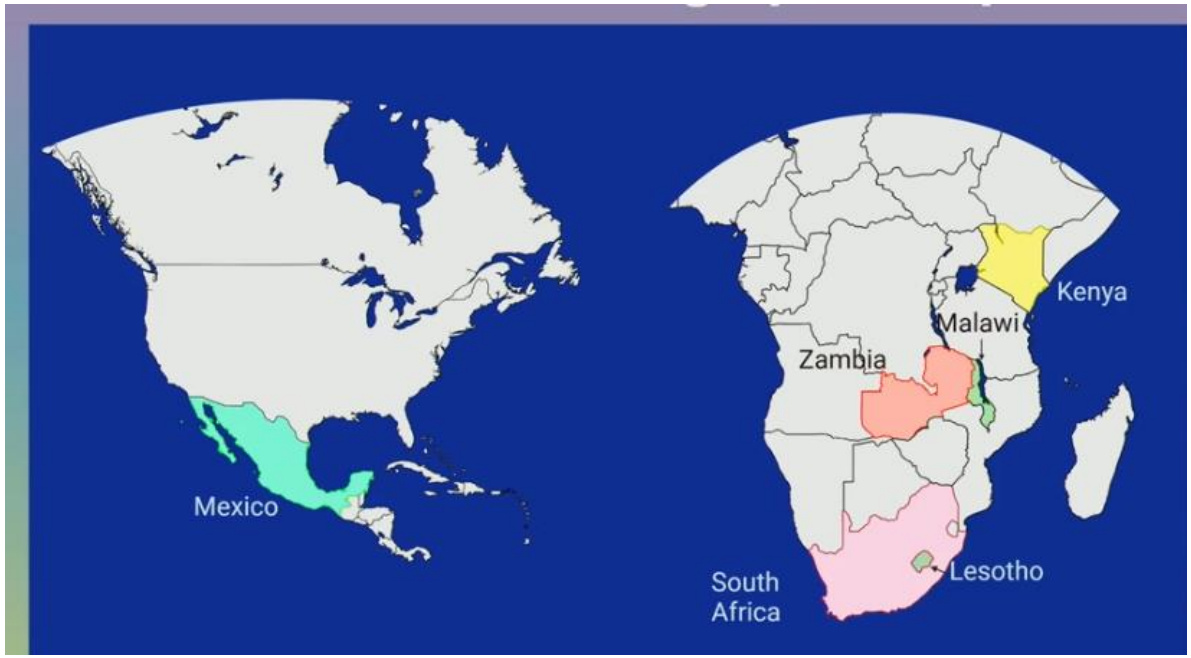
Adverse events (incidence for 100 patient-years)

	B/F/TAF N = 220	D/c/F/TAF N = 222	Adjusted IRR	p
All AE grade ≥ 2	220.5	264.7	0.82 (0.73 – 0.93)	0.024
AE related to treatment grade ≥ 2	13.7	21.7	0.61 (0.38 – 0.98)	0.043
AE related to treatment grade 3-4	2.5	2.4	0.99 (0.29 – 3.44)	0.99

- **Conclusion:** in patients with advanced HIV infection (AIDS, CD4 < 100/mm^3), for first-line ART, BIC/F/TAF
  - Is non-inferior to DRV/c/F/TAF
  - Achieves better virologic response and leads to less adverse events at W48

Behrens G, CROI 2025, Abs. 658

Is resistance to INSTIs common?



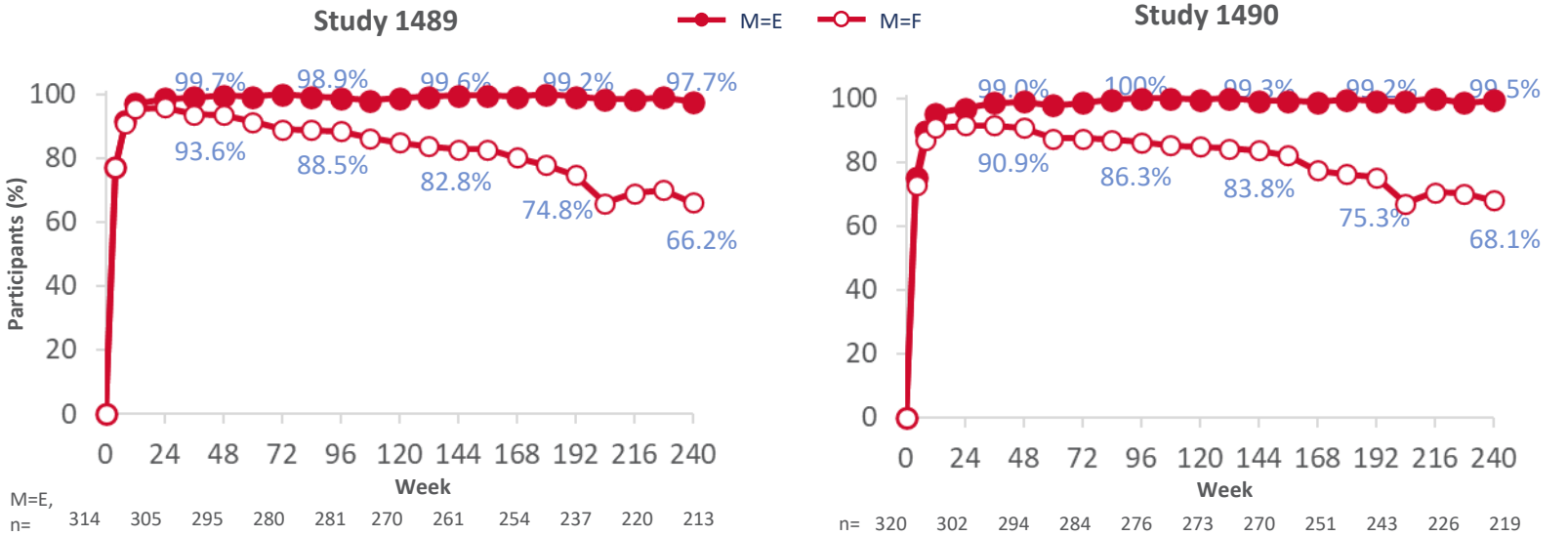
Resistance to DTG being reported but rates well below <1% on population scale

CROI 2024

B/F/TAF Resistance in Naives with VF

5-year virological outcomes

rates of virological suppression[a] (M=E and M=F) through
<u>five years</u> of follow-up among TN PLWH originally randomised to B/F/TAF



- Median CD4 changes from B/F/TAF start to Week 240, cells/µL (IQR): Study 1489: +313 (179, 475); Study 1490: +331 (215, 467)

<u>No treatment-emergent resistance on B/F/TAF detected in VF out to 5 years</u>

[a] HIV-1 RNA <50 copies/mL calculated using FDA Snapshot algorithm; includes only participants initially randomised to B/F/TAF M=E: missing=excluded; M=F: missing=failure; TN: treatment-naïve; PLWH: people living with HIV.
Wohl D, *et al.* CROI 2022 (Poster 494)

DTG Resistance in naives with VF

96 Wk After Open-Label Switch to BIC/FTC/TAF in Extension of Studies 1489 and 1490

Resistance, n	DTG/ABC/3TC → BIC/FTC/TAF (n = 254)	DTG + FTC/TAF → BIC/FTC/TAF (n = 265)
Met criteria for resistance testing*	3	1
NRTI resistance detected	0	0
INSTI resistance detected	0	0

*Resistance testing done for participants with confirmed HIV-1 RNA ≥200 c/mL or HIV-1 RNA ≥200 c/mL at last visit without resuppression to HIV-1 RNA <50 c/mL while on study drug.

2 participants on blinded DTG/ABC/3TC had HIV-1 RNA ≥200 copies/mL at time of switch to BIC/FTC/TAF

- **Both later found to have M184V and resuppressed on open-label BIC/FTC/TAF**

Orkin. HIV Glasgow 2022. Abstr P088.

DTG RESIST Study
HIV-1 Resistance in People on Dolutegravir-Based ART

- Cohorts with INSTI genotype resistance data (n=599)
  - Dolutegravir-based ART (**initial**/switch regimens): 81%
    - **≥19%/**3 antiretrovirals (85%); non-3TC (9%); 3TC (3%), monotherapy (3%)
- Fully susceptible to dolutegravir: 94%
- INSTI mutations detected: 14%
- Dolutegravir drug resistance: 6%
  - **Higher risk associated with dolutegravir monotherapy, dolutegravir/3TC dual therapy, and NRTI resistance**
  - **Monitoring is important to prevent resistance!**

Cohorts: ART Cohort Collaboration, International epidemiology Databases to Evaluate AIDS in Southern Africa, UK Collaborative HIV Cohort
Resistance levels were categorized using the Stanford algorithm.

Odds Ratios for Dolutegravir Resistance (Multivariate Analysis)

	Adjusted Odds Ratio (95% CI)
ART regimen (reference ≥3 drugs)	
Dual ART (other)	1.74 (0.43-7.01)
Dual therapy (3TC)	9.21 (2.20-38.55)
Monotherapy	34.09 (9.93-117.01)
NRTI resistance (reference: susceptible)	
Low	5.23 (1.32-20.71)
Intermediate and high	13.44 (4.55-39.68)
RT not sequenced	1.61 (0.50-5.19)

Adjusted for sex, age at initiation, time on dolutegravir-based ART, HIV-1 subtype, type of ART, exposure to 1st generation INSTI, HIV RNA level, viral load testing frequency, resistance to NRTIs.

Loosli T, et al. *Lancet HIV.* 2023;10:e733-e741.

Resistance data across real-world cohorts in LMICs (#1)

Study	N	Population	Timepoint/s	Results
Wagude J, et al.[1] Kenya	• Referred for testing: N=209 • Successful GRT: n=98	• Adults and children experiencing virological failure on DTG-based regimens • VL >1,000 c/mL	GRT was conducted between Jul 2020 and Oct 2024	• Of individuals with viremia on DTG-based ART referred for GRT, 22 (11%) had DTG resistance (15 [68%] with high-level and 5 [23%] with intermediate-level resistance) • Of those with DTG resistance, 19 (86%) were treatment-experienced with DRMs and 3 (14%) were ART-naïve • Before HIVDR testing, 14 (64%) had never been virologically suppressed on DTG • Following treatment switch, 12 individuals (55%) had virologic suppression (VL <50 c/mL), 6 (27%) had VL >1,000 c/mL and 2 (9%) died
Ainembabazi B.[2] Uganda	6,311	• 53% female with a median age of 22 years (IQR 14–39) • 43% spent 6–10 years on ART (n=1,795) • 52% on first line ART (n=3,313)	Retrospective cohort of all individuals whose samples were sent for HIVDR testing between Apr 2021 and Mar 2023	• Individuals with HIVDR accounted for 351 cases (5.6%) • HIVDR increased by 6% between Jul−Sept 2021 and Jul−Sept 2023, followed by a 2% decline by Jan−Mar 2024 (p=0.012) • INSTI resistance increased from 0 to 29% between Apr−Jun 2021 and Apr−Jun 2023, respectively, and declined by 6% by Jan−Mar 2024 (p=0.013)
DREAM Program[3] Mozambique	13	• Individuals experiencing virological failure on DTG	NR	• DTG-associated resistance mutations (between 1 and 5) presented in 9 individuals (69%) • G118R and E138K were the most frequent mutations (in 5 individuals each) • RTI-resistance was prevalent among those with DTG-resistance; no PI resistance was observed • Prior treatment failure was more common among individuals with DTG resistance versus those without (67% vs 13%, respectively)
RV254/ SEARCH010 cohort[4] Thailand	• **[A]** With acute HIV infection, TDRM prior to ART initiation: N=304 • **[B]** After VF while on DTG-based ART: N=32	• 98% and 97% male in A and B, respectively • Median age 27 years (IQR 23–32), and 24.5 (IQR 22.5–28), respectively	Individuals diagnosed and initiated ART during acute HIV infection; followed up to 20 years	• Prevalence of Transmitted DRM (INSTI) decreased from 4.8% to 0% over 6 years • Prevalence of Acquired DRM (INSTI) was rare after VF (16.7% reduced to 0% after 1 year) • E138K and Y143FY constituted the major DRMs

DTG resistance cases occurred mostly in treatment-experienced individuals with repeated non-suppressed viral loads and prior ART failure; overall DTG resistance remains low

See next slide for references

Resistance data across real-world cohorts in LMICs (#2)

Study	N	Population	Timepoint/s	Results
Msafiri F, et al.[1] Tanzania	Eligible children (<15 years): n=388 Eligible adults (≥15 years): n=919	• HIV VL ≥1,000 c/mL • Receiving DTG-based ART for ≥9 months	First round of CADRE surveillance conducted in Apr−Sept 2023	• Among children, 8.3% had clinically significant DTG resistance (5.5% high-level resistance), and 36% had clinically significant NNRTI and 31.8% had NRTI resistance, respectively • Among adults, 5.1% had clinically significant DTG resistance (3.3% high-level resistance), and 22% had clinically significant NNRTI and 8.8% had NRTI resistance, respectively • Most common INSTI DRMs among both children and adults were G118R, Q148K/R and R263K
Pheng P, et al.[2] Cambodia	312 Samples with VL >1,000 c/mL that underwent HIV sequencing: n=273	• ART-naïve • Median age 30 years (IQR 25–38) • 78.5% male at birth; 5.1% trans women	Mar−Aug 2024	• Overall pretreatment drug resistance prevalence was 19.5%: 10.2% NRTI resistance, 3.5% NNRTI resistance and 9.9% PI resistance • No DTG-associated resistance mutations were observed • Most frequent NNRTI mutation was E138A, and PI resistance mutations were highly prevalent
Ssentongo S, et al.[3] Uganda	225	• Individuals receiving DBRs with ≥2 VL counts >1,000 c/mL, who had HIVDR testing • 55.1% male • Median age 19 years (IQR 15–39)	Apr 2022–Jul 2024	• Individuals with intermediate- to high-level DTG resistance accounted for 50 cases (22.2%) • Intermediate- to high-level DTG resistance was associated with NRTI resistance, poor adherence, alcohol and substance abuse, and family dysfunction

DTG resistance cases occurred mostly in treatment-experienced individuals with repeated non-suppressed viral loads and prior ART failure; overall DTG resistance remains low

References:

1. Wagude J, et al. IAS 2025. Poster THPEB019
2. Ainembabazi B. IAS 2025. Poster EP0060
3. Ciccacci F, et al. IAS 2025. Poster EP0061
4. Promsena P, et al. IAS 2025. Poster EP0063

Intensification

Original Research | 11 February 2020

Addition of Maraviroc Versus Placebo to Standard Antiretroviral Therapy for Initial Treatment of Advanced HIV Infection: A Randomized Trial

Authors: Yves Lévy, MD, PhD, Jean-Daniel Lelièvre, MD, PhD, Lambert Assoumou, PhD, Esther Aznar, MD, Federico Pulido, PhD, Giuseppe Tambussi, MD, Manuel Crespo, PhD, ... SHOW ALL ... , and Dominique Costagliola, PhD | AUTHOR, ARTICLE, & DISCLOSURE INFORMATION

Publication: Annals of Internal Medicine • Volume 172, Number 5 • https://doi.org/10.7326/M19-2133

- 416 HIV-positive, antiretroviral-naive adults with CD4 counts less than 0.200×10^9 cells/L and/or a previous AIDS-defining event (ADE).
- C-ART plus placebo or maraviroc (300 mg twice daily with dose modification) for 72 weeks.
- The primary end point was first occurrence of severe morbidity (new ADE, selected serious infections, serious non-ADE, immune reconstitution inflammatory syndrome, or death). Prespecified secondary outcomes included primary outcome components, biological and pharmacokinetic measures, and adverse events graded 2 or higher.

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- **Results**

- 409 randomly assigned participants (207 in the placebo group and 202 in the maraviroc group) who received more than 1 dose were included in the analysis. During 72 weeks of follow-up, incidence of **severe morbidity was 11.1 per 100 person-years in the maraviroc group** and **11.2 per 100 person-years in the placebo group** (hazard ratio, 0.97 [95% CI, 0.57 to 1.67]). Incidence of adverse events graded 2 or higher was 36.1 versus 41.5 per 100 person-years (incidence rate ratio, 0.87 [CI, 0.65 to 1.15]).

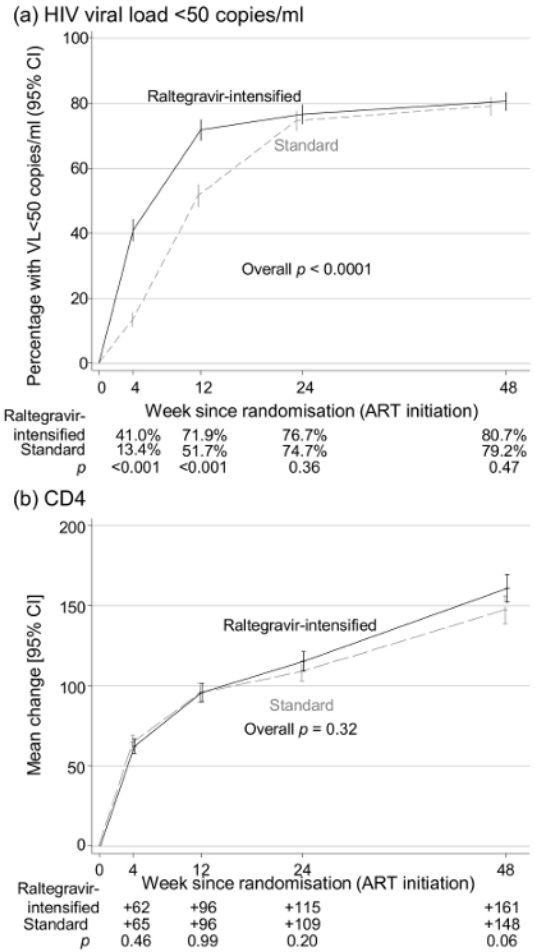
Intensification

RESEARCH ARTICLE

Raltegravir-intensified initial antiretroviral therapy in advanced HIV disease in Africa: A randomised controlled trial

Cissy Kityo[1], Alexander J. Szubert[2], Abraham Siika[3], Robert Heyderman[4,5], Mutsa Bwakura-Dangarembizi[6], Abbas Lugemwa[7], Shalton Mwaringa[8], Anna Griffiths[2], Immaculate Nkanya[1], Sheila Kabahenda[9], Simon Wachira[3], Godfrey Musoro[6], Chatu Rajapakse[2], Timothy Etyang[8], James Abach[10], Moira J. Spyer[2], Priscilla Wavamunno[1], Linda Nyondo-Mipando[4], Ennie Chidziva[6], Kusum Nathoo[6], Nigel Klein[11], James Hakim[6], Diana M. Gibb[2€*], A. Sarah Walker[2€*], Sarah L. Pett[2,12,13€], on behalf of the REALITY trial team[¶]

PLoS Medicine 2018



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PLoS Medicine 2018

- **Conclusions**

- Although 12 weeks of raltegravir intensification was well tolerated and reduced HIV viraemia significantly faster than standard triple-drug ART during the time of greatest risk for early death, this strategy did not reduce mortality or clinical events in this group and is not warranted. There was no excess of IRIS-compatible events, suggesting that integrase inhibitors can be used safely as part of standard triple-drug first-line therapy in severely immunocompromised individuals.

Conclusions

- Late presentation is common and not decreasing over time
- The impact of LP are personal and immunological and at a population level.
- Late presenters need rapid start
- Choice of drug therapy is clearer with recent LAPTOP study
- Patients who are LTFU and represent late are complex
- Intensification does not add an extra value