Rapid ART

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Disclosures

Grants for educational activities, personal fees for advisory boards and speakers bureau in last 2 years

- Gilead Sciences
- Janssen-Cilag
- ViiV Healthcare
- Pfizer

Study grant/support to my institution in last 2 years

- Gilead Sciences

Immediate antiretroviral therapy

- Starting HIV treatment as soon as possible after the diagnosis of HIV infection

Rapid ART

Test & treat

Treatment upon diagnosis

Same-day ART

Undetectable Viral Load Equals Untransmittable HIV Infection (U=U)

- In 2017, HIVMA officially endorsed the U=U Consensus Statement
  - "When a person living with HIV has an undetectable viral load, they will not transmit HIV"
- In 2019, in Italy…

https://www.hivma.org

- Supported by data from several studies from 2008-2016 showing zero linked HIV transmissions after >100,000 condomless sex acts within both female–male and male–male serodiscordant couples in which the partner with HIV had a **durably undetectable viral load**

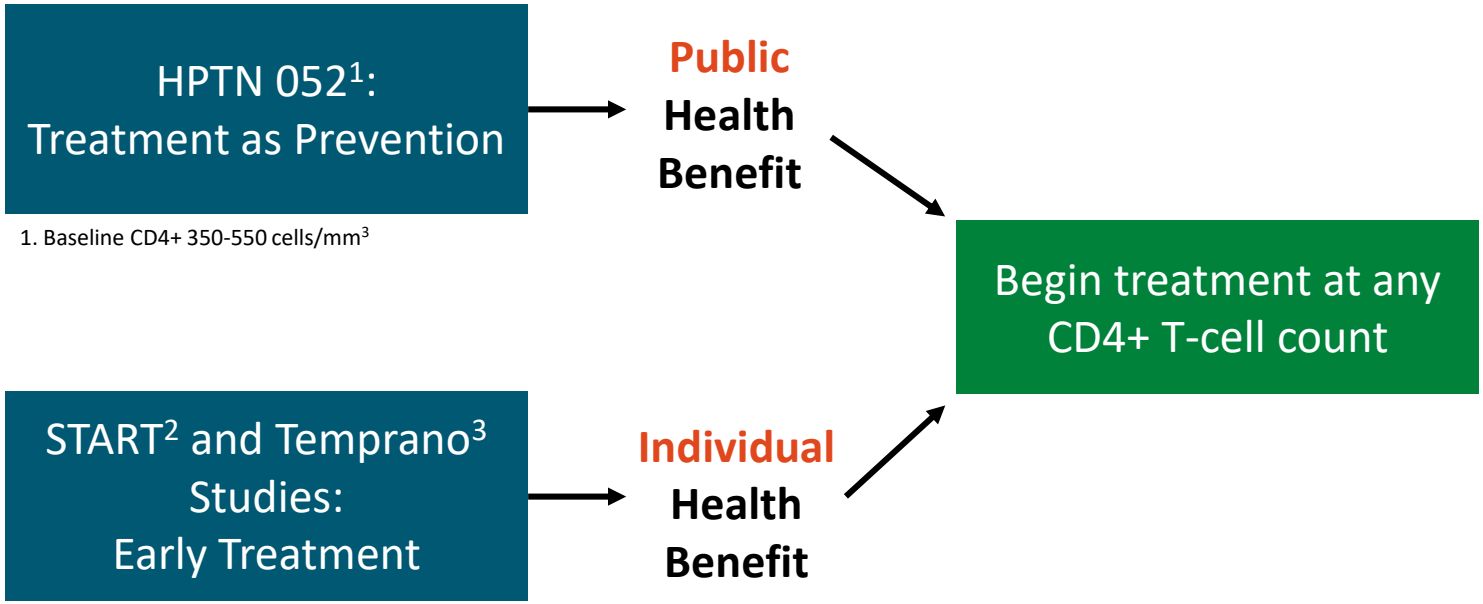
HPTN 052

PARTNER

Opposites Attract

PARTNER 2

Early ART Initiation: Individual and Public Health Benefit



1. Baseline CD4+ 350-550 cells/mm^3

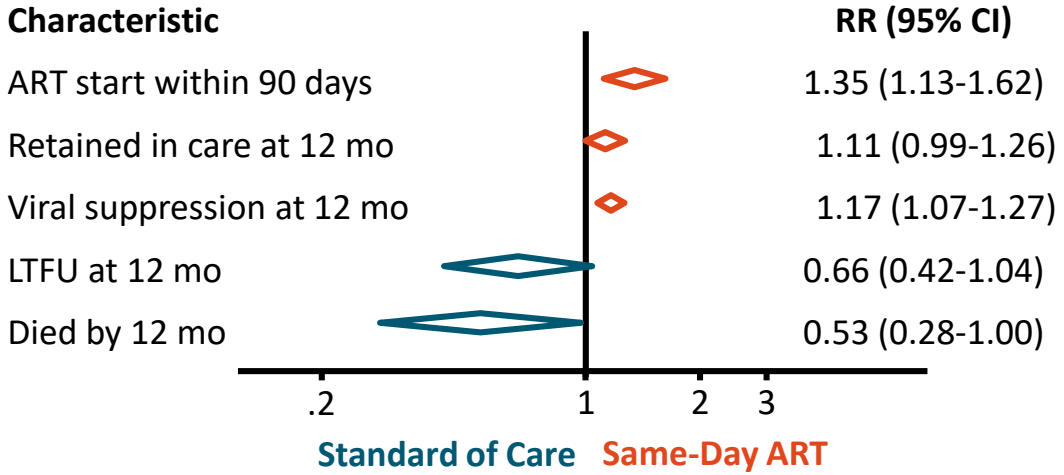
2. Baseline CD4+ >500 cells/mm^3

3. Baseline CD4+ <350 cells/mm^3

1. Cohen. NEJM. 2011;365:493. 2. INSIGHT START Study Group. NEJM. 2015;373:795.
3. TEMPRANO ANRS 12136 Study Group. NEJM. 2015;373:808.

Improved Clinical Outcomes With Rapid ART Initiation

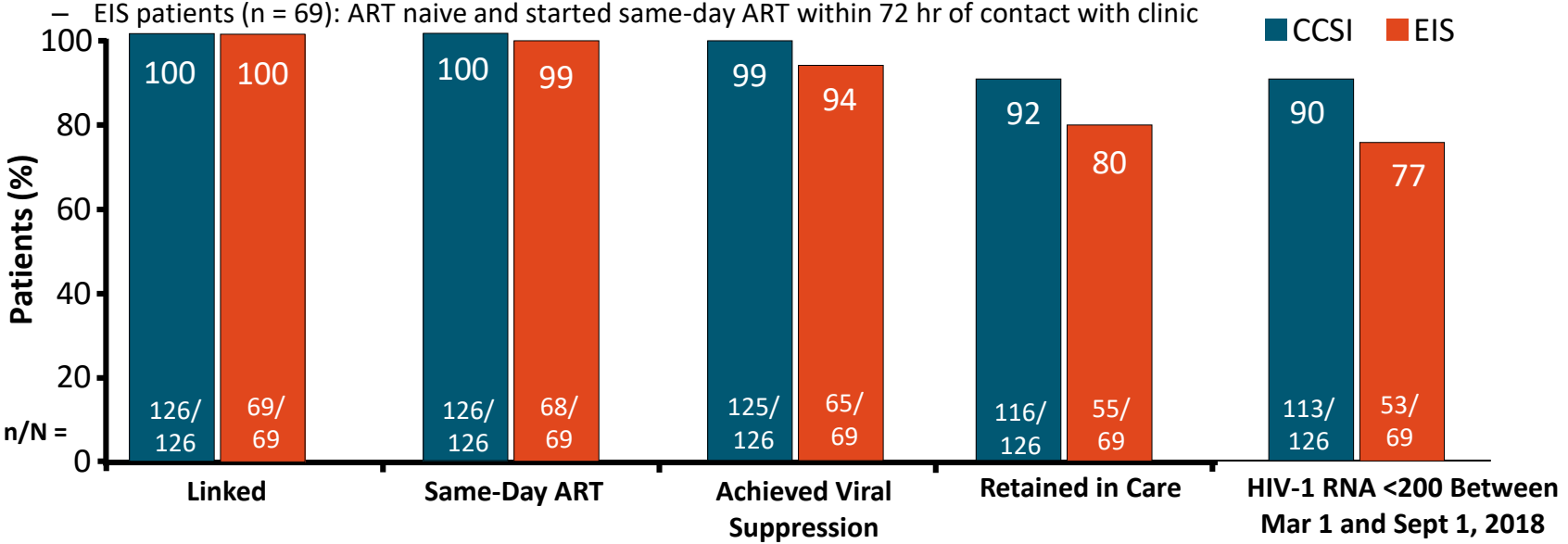
- Systematic review[1] of ART initiation within 14 days of eligibility determination across 4 randomized clinical trials in **Uganda,[2] South Africa,[3] Haiti,[4] and Lesotho[5]**
- Compared with standard of care, **same-day ART increased the** likelihood of ART initiation in first 90 days, patient retention, and viral suppression at 12 mo



1. Ford. AIDS. 2018;32:17. 2. Amanyire. Lancet HIV. 2016;3:e539. 3. Rosen. PLoS Med. 2016;13:e1002015.
4. Koenig. PLoS Med. 2017;14:e1002357. 5. Labhart. BMC Public Health. 2016;16:329.

CrescentCare Start Initiative

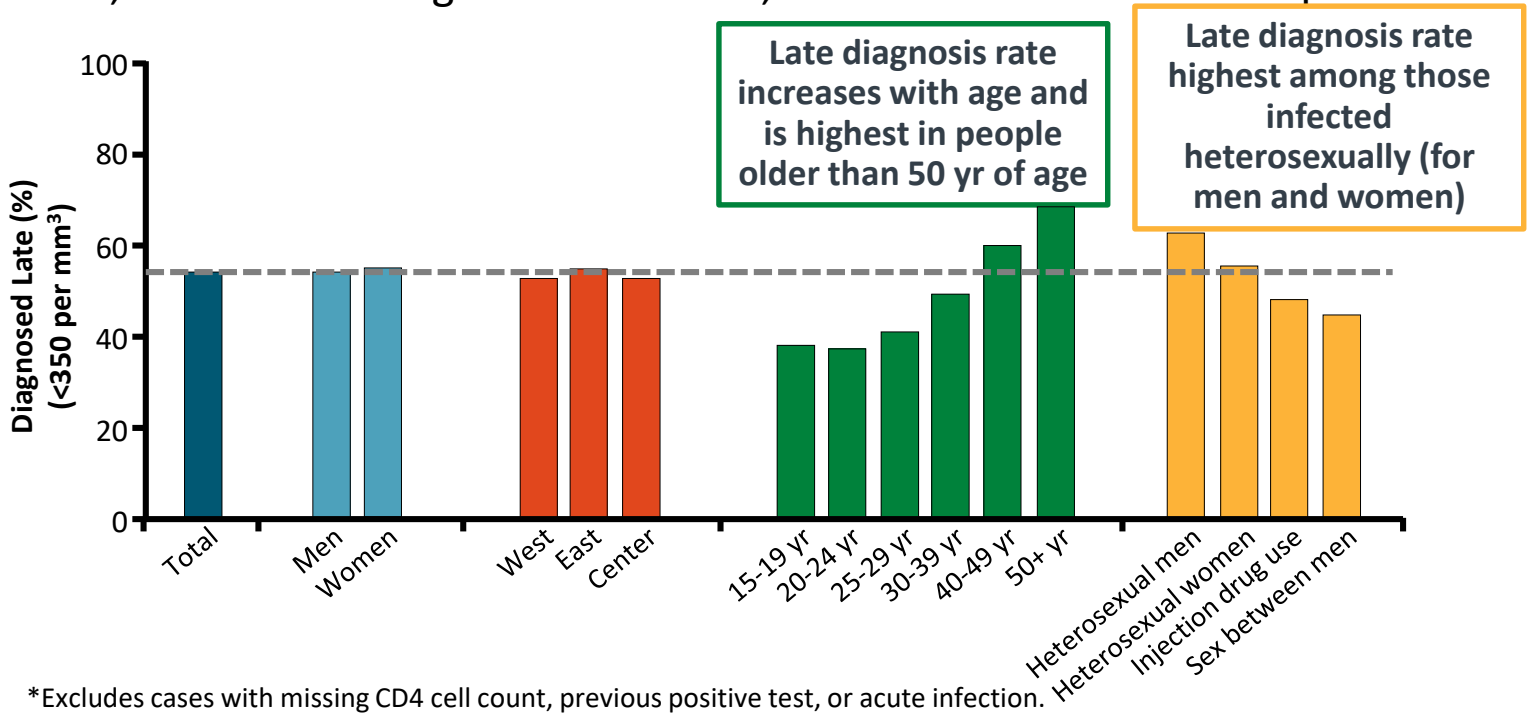
- All patients started on TAF/FTC + DTG (December 2016 - February 2018):
  - CCSI patients (n = 126): linked and same-day ART within 72 hr of diagnosis
  - EIS patients (n = 69): ART naive and started same-day ART within 72 hr of contact with clinic



Halperin. Open Forum Infect Dis. 2019;6:ofz161

Late HIV Diagnosis Remains a Challenge in Europe and Varies by Mode of Transmission and Age

- In 2021, 54% of new diagnoses were late, with CD4 cell counts <350 per mm^3*



*Excludes cases with missing CD4 cell count, previous positive test, or acute infection.

HIV/AIDS Surveillance in Europe. 2022. ecdc.europa.eu/sites/default/files/documents/2022-Annual_HIV_Report_final.pdf.

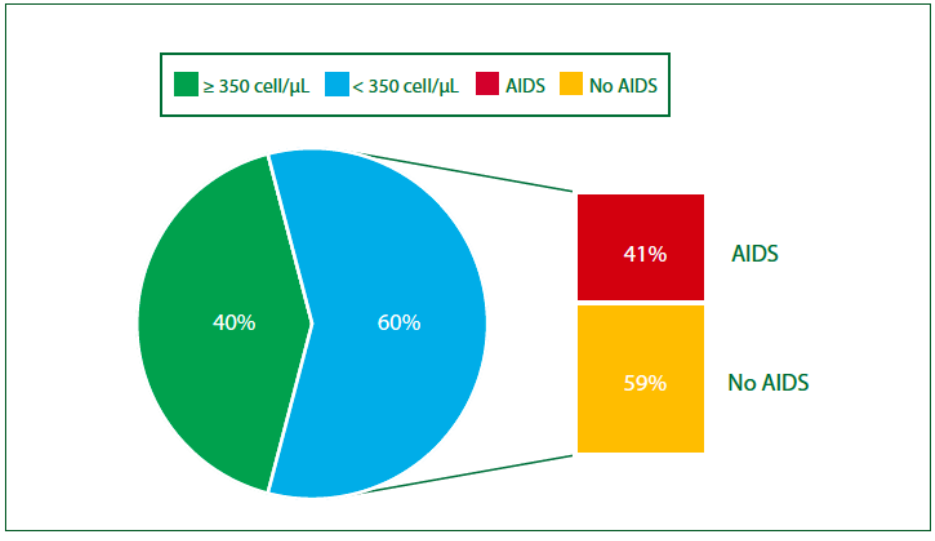


Figura 12 - Proporzione delle nuove diagnosi di infezione da HIV per numero di linfociti CD4 e diagnosi di AIDS (2023)

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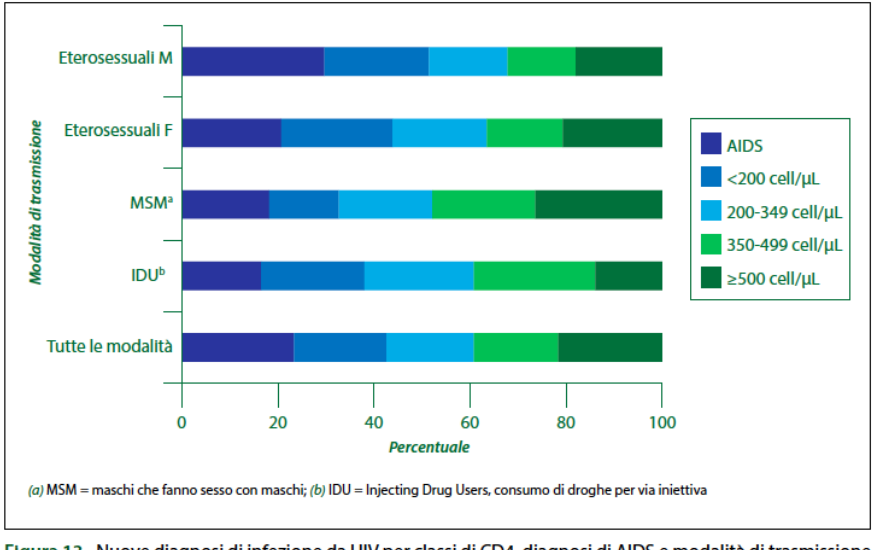
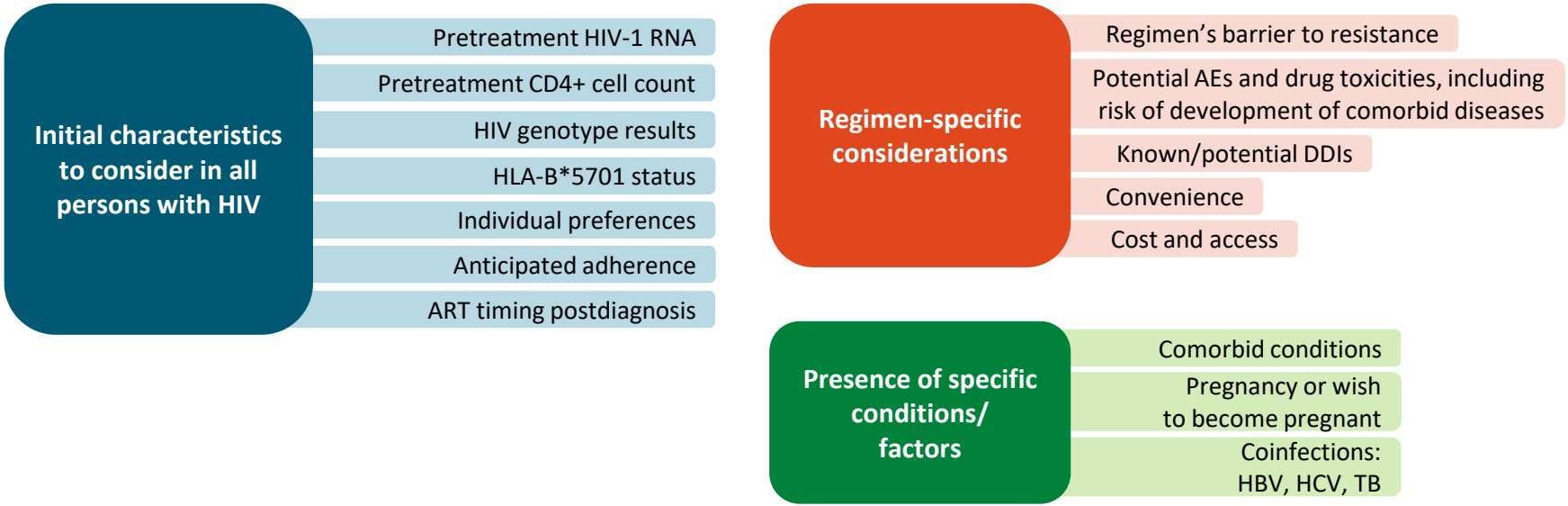


Figura 13 - Nuove diagnosi di infezione da HIV per classi di CD4, diagnosi di AIDS e modalità di trasmissione (2023)

Selecting Initial ART: Factors to Consider



Discuss ART options with patients to determine their needs and extent to which they want to be involved in decision-making

clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf

Patient Information Before Initiating Rapid ART

Needed Prior to Start

- Patient prepared for ART and interested in rapid initiation
- Physical examination
  - Active cryptococcal meningitis or TB infection could increase risk for IRIS and *may warrant a short ART delay*
  - Other AIDS-defining conditions could increase risk of morbidity/mortality if therapy is delayed
- Counsel on medication adherence

NOT Needed Prior to Start

- CD4 cell count
- HIV-1 RNA
- HIV genotype
- Drug-resistance test results
- Hepatitis B/C status
- HLA-B*5701 status
- STI screening results
- Pregnancy test results

DHHS Guidelines. 2023. WHO. Consolidated Guidelines On HIV Prevention, Testing, Treatment, Service Delivery and Monitoring. 2021.

Recommendations for Rapid ART

Guideline	Recommendation for Rapid ART
DHHS[1]	**Initiate ART immediately (or as soon as possible)** after HIV diagnosis to increase uptake of ART and linkage to care, decrease time to viral suppression for individual patients, and improve rate of virologic suppression among people with HIV
IAS-USA[2]	Initiation of ART is recommended **as soon as possible after diagnosis,** ideally within 7 days, including on same day as diagnosis or at first clinic visit if **patient is ready**
EACS[3]	**Immediate (ie, same-day) start of ART should be considered,** especially in the following situations: primary HIV infection, wish to start ART immediately, in a setting where loss to follow-up is more likely if ART is not started on same day
WHO[4]	**Rapid ART initiation should be offered to all people with HIV** following confirmed HIV diagnosis and clinical assessment

1. DHHS ART Guidelines. 2024. 2. Gandhi. JAMA. 2024. 3. EACS Guidelines. V12.1. 2024. 4. WHO Guidelines. July 2021.

Guideline Recommendations for Initial ART

DHHS[1]	IAS-USA[2]	EACS[3]
▪ **BIC**/FTC/TAF ▪ **DTG** + (3TC or FTC) + (TAF or TDF) ▪ **DTG**/3TC‡ ▪ **DRV/c** or **DRV/r** + (3TC or FTC) + (TAF or TDF)*	▪ **BIC**/FTC/TAF ▪ **DTG** + (3TC or FTC) + (TAF or TDF) ▪ **DTG**/3TC‡	▪ **BIC**/FTC/TAF ▪ **DTG** + FTC/TAF or (3TC or FTC)/TDF ▪ **DTG**/3TC or **DTG** + (3TC or FTC)‡ ▪ **DOR**/3TC/TDF or **DOR** + FTC/TAF or (3TC or FTC)/TDF§
‡Except for persons with baseline HIV-1 RNA >500,000 c/mL, with HBsAg+, or pending HIV genotypic resistance test ***For people who have CAB-LA as PREP failure, pending genotypic resistance testing results**	‡Except for persons with baseline HIV-1 RNA >500,000 c/mL, with HBsAg+, or pending HIV genotypic resistance test or in lamivudine resistance	‡Except for persons with baseline HIV-1 RNA >500,000 c/mL, with HBsAg+, or after PREP failure § DOR is not active against HIV-2. Results of genotypic resistance test are necessary before to start DOR-including regimen

1. DHHS Guidelines. 2024. 2. Gandhi. JAMA. 2024. 3. EACS Guidelines. v.12.1 2024.

Regimens for Same-Day ART

Recommended

- **BIC**/FTC/TAF*
- **DTG** + (3TC or FTC) + (TAF or TDF)*
- (**DRV**/RTV or **DRV**/COBI) + (3TC or FTC) + (TAF or TDF)

NOT Recommended

- NNRTI-based regimens (possible transmitted drug resistance)
- **DTG**/3TC

Key Features of Same-Day ART Regimens:

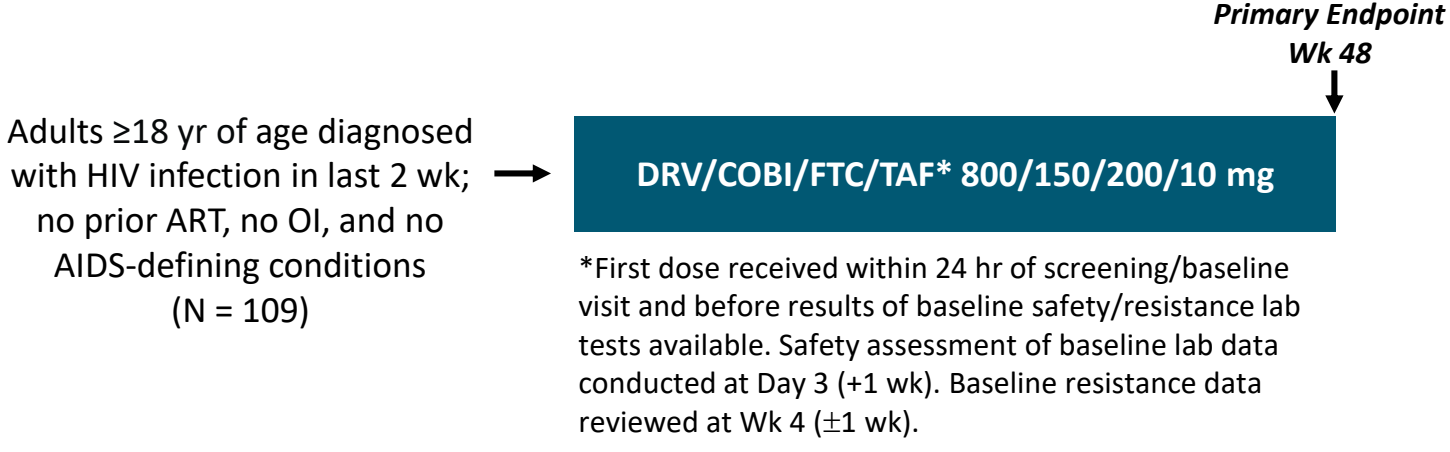
- High barrier to resistance (in case there is transmitted drug resistance)
- Activity against HBV
- Can be used without HLA-B*5701 test result

DHHS Guidelines. 2024.

*Not recommended if receiving LA CAB for PrEP prior to HIV acquisition pending genotypic resistance test results

DIAMOND: Rapid Initiation of DRV/COBI/FTC/TAF

- Prospective, multicenter, open-label, single-arm phase III study to assess efficacy and safety of single-tablet regimen for rapid start ART

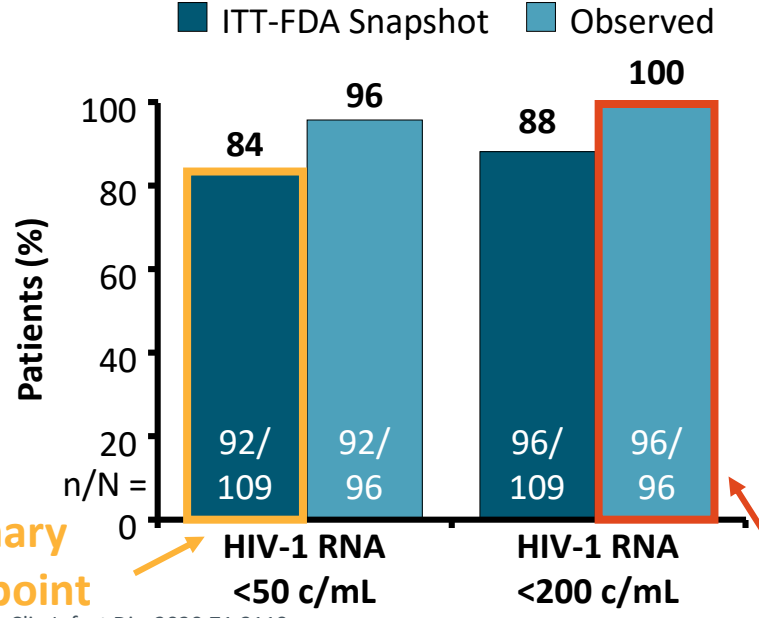


- Primary endpoint: virologic response in ITT at Wk 48 by FDA snapshot (HIV-1 RNA <50 copies/mL)

Huhn. Clin Infect Dis. 2020;71:3110.

DIAMOND: High Virologic Suppression Through Wk 48 Regardless of Baseline HIV-1 RNA, CD4+ Cell Count

- No patient met criteria for PDVF or d/c for lack of efficacy
- No drug-related serious AEs; d/c for drug-related AE: n = 1 (allergic dermatitis)



HIV-1 RNA <50 c/mL by Subgroup, % (n/N)	ITT-FDA Snapshot	Observed
Baseline HIV-1 RNA		
▪ <100,000 c/mL	89 (72/81)	99 (72/73)
▪ ≥100,000 c/mL	70 (19/27)	86 (19/22)
Baseline CD4+ cell count		
▪ ≤200 cells/mm^3	74 (17/23)	90 (17/19)
▪ >200 cells/mm^3	87 (74/85)	97 (74/76)

Huhn. Clin Infect Dis. 2020;71:3110.

Virologic Efficacy and Tolerance of Rapid Start With BIC/FTC/TAF in PWH With Primary HIV Infection

- Retrospective, cohort study in France
  - Primary outcome: HIV-1 RNA <50 c/mL at Wk 48

Baseline Characteristics	BIC/FTC/TAF (N = 11)
Median age, (range)	37 (26-47)
Male sex, %	91
Median CD4 + cells, cells/mm^3 (range)	485 (290-1060)
Median HIV-RNA, log_{10} copies/mL, (range)	5.5 (3.9-7.9)
▪ >100,000 copies/mL, n	8
Median BMI, kg/m^2 (range)	23 (18-34)

- Median delay between first consultation and B/F/TAF start: 1 day (range 0–11)

- By 48 wk:
  - 100% of participants met the primary endpoint
  - No grade 3/4 AEs; no treatment d/c due to TRAE reported
- BIC/FTC/TAF initiated at time of primary HIV infection appeared to be safe and yielded rapid virologic suppression

Bachelard. J Antimicrob Chemother 2021;76: 2484.

Rapid ART initiation with bictegravir/emtricitabine/tenofovir alafenamide in individuals presenting with advanced HIV disease (RAINBOW study)

Our results support the efficacy, feasibility and safety of BIC/FTC/TAF as a rapid ART strategy in patients with advanced HIV disease

Background: a rapid ART initiation approach can be beneficial in people with advanced HIV disease[1,2] for their high morbidity and mortality[3,4].

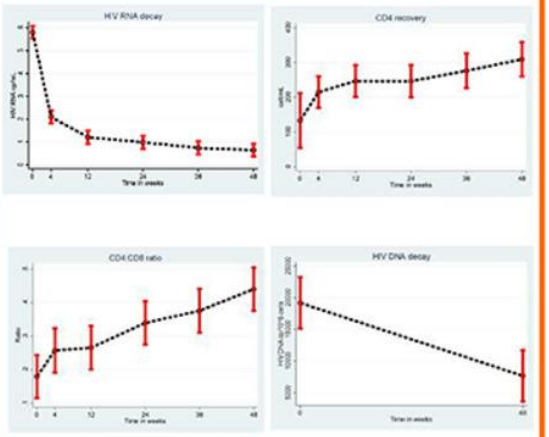
Study design: Pilot, single center, phase IV, clinical trial.

Aim: to evaluate the efficacy, feasibility and safety of rapid ART start BIC/FTC/TAF in advanced HIV disease.

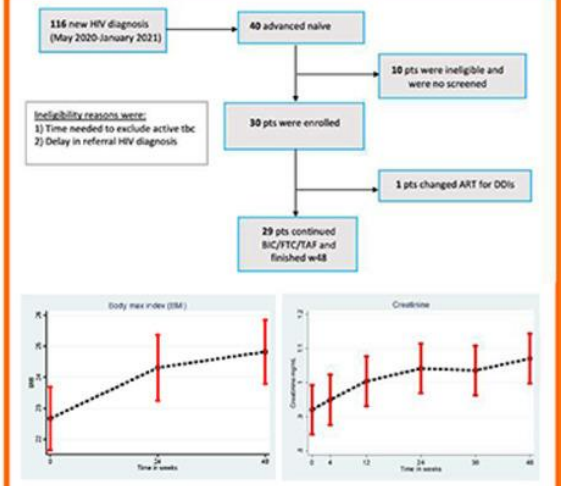
Population: 30 ART-naïve people presenting with AIDS-defining event and/or CD4 cell count <200 µL.

Endpoints: 1) clinical or virologic failure **2)** immunological parameters, safety and feasibility.

Procedures: BIC/FTC/TAF 50/200/25 mg was started within 7 days. *Timepoints:* BL, w4, w12, w 24, w36, w48.



2 unconfirmed VF and 1 clinical failure occurred. No ART discontinuation due to toxicity, VF or GRT mutations was observed.



Adverse Events	At least possibly related
Any	15
Grade 1	8
Grade 2	5
Grade 3	0
Grade 4	0
Serious AE	2

Marta Camici MD, PhD & Roberta Gagliardini MD National Institute for Infectious Diseases L. Spallanzani, Rome, IT.

1.Antinori et al. HIV Medicine, 2011; ECDC 2017.
2.Raffetti et al. BMC public Health 2016.
3.Egger et al. Lancet, 2002.
4.Zolopa et al. Plos One, 2009.

Int J Antimicrob Agents. 2024

STAT Study: Rapid Test-and-Treat With DTG/3TC in Adults With Newly Diagnosed HIV

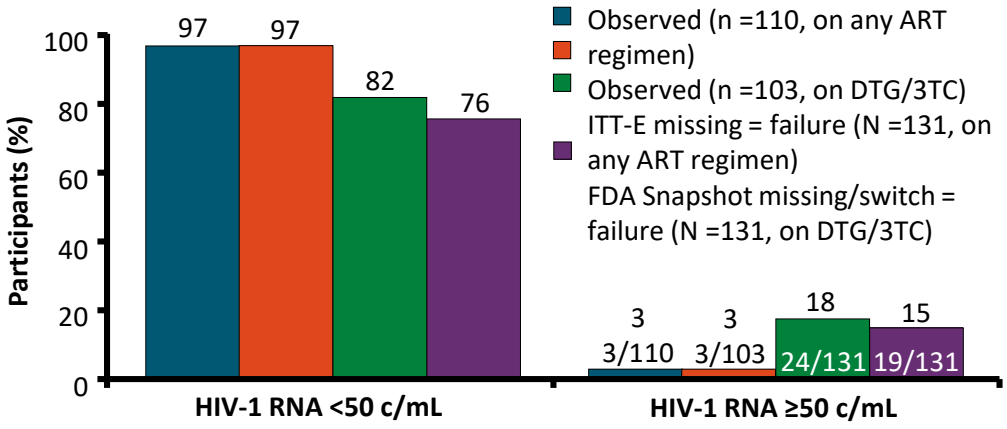
- Dual therapy with DTG + 3TC has demonstrated long-term efficacy that is noninferior to triple therapy with DTG + FTC/TDF as first-line ART[1]
- STAT: multicenter, open-label phase III study of DTG/3TC in rapid test-and-treat protocol[2]

Baseline HIV-1 RNA c/mL, n (%)[3]	DTG/3TC
Median c/mL, range	63,056 (<40-68,706,840)
▪ <100,000	79 (60)
▪ 100,000- <500,000	32 (24)
▪ 500,000- <1,000,000	9 (7)
▪ ≥1,000,000	10 (8)

1. Cahn. JAIDS. 2020;83:310. 2. NCT03945981. 3. Rolle. IAS 2021. Abstr PEB182.

STAT Study: Rapid Initiation of DTG/3TC
Wk 48 Results

Virologic Outcomes at Wk 48



Participants Who Switched From DTG/3TC by Wk

Reasons for Switch	Visit Window	Modified ART	Plasma HIV-1 RNA at Wk 48, c/mL
BL HBV	Wk 1	DTG/3TC + TAF	<40
BL HBV	Wk 1	BIC/FTC/TAF	<40
BL HBV	Wk 4	DTG + TAF/FTC	<40
BL HBV	Wk 4	BIC/FTC/TAF or DTG + TDF/FTC	N/A
Decision by participant or proxy	Wk 4	BIC/FTC/TAF	N/A
BL HBV	Wk 8	DTG/3TC + TAF	<40
BL M184V	Wk 8	DTG/RPV	N/A
AE (rash)	Wk 12; Wk 12	DRV/COBI/FTC/TAF; BIC/FTC/TAF‖	<40
Decision by participant or proxy	Wk 24	BIC/FTC/TAF	<40
Pregnancy	Wk 24	DTG/ABC/3TC	327; <40

Rolle. IAS 2021. Abstr PEB182.

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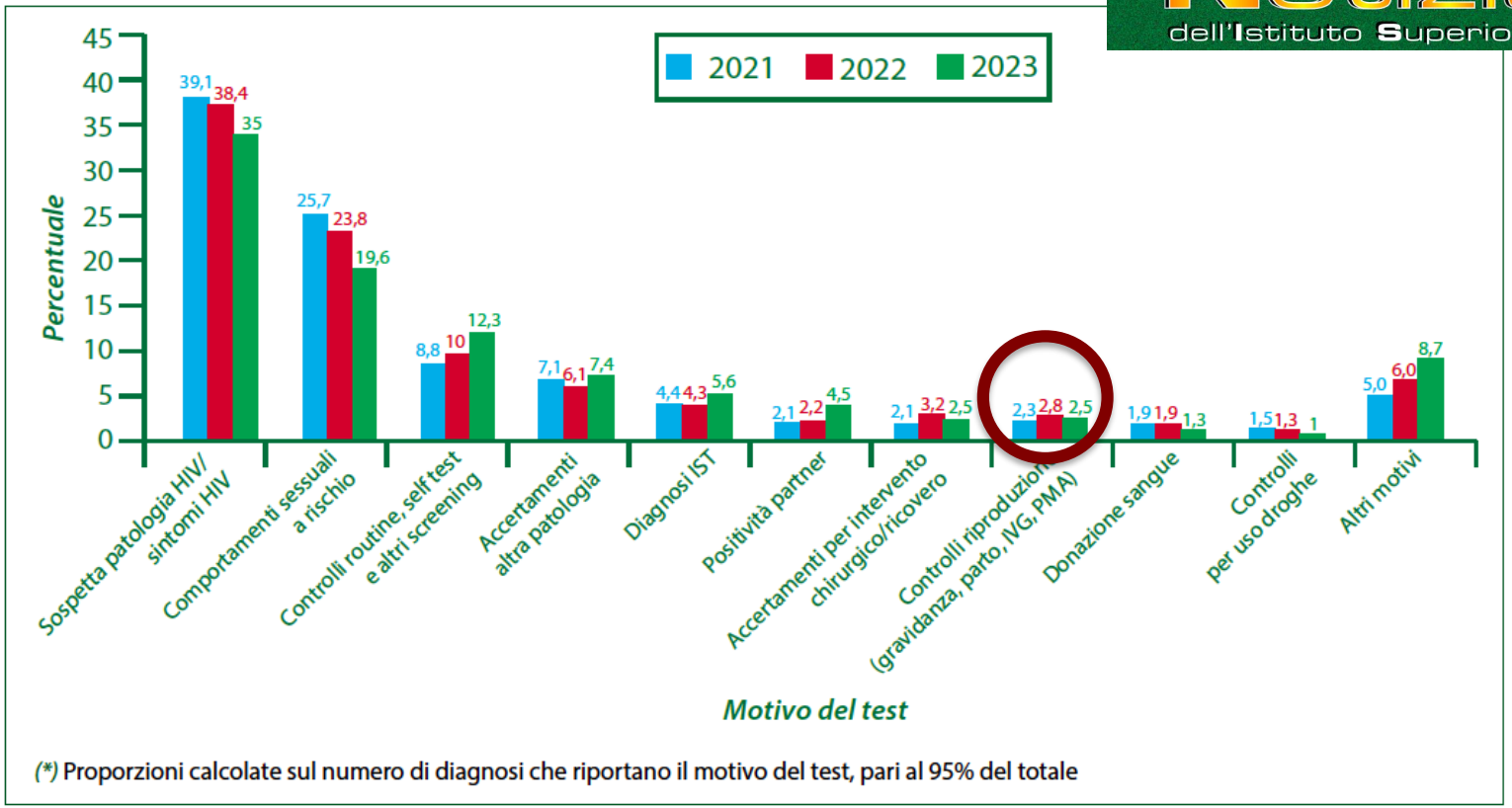


(*) Proporzioni calcolate sul numero di diagnosi che riportano il motivo del test, pari al 95% del totale

Figura 15 - Nuove diagnosi per motivo di effettuazione del test HIV* (2021-2023)

Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy

- ART-naïve pregnant women **should initiate treatment as soon as possible**.
- The **decision of ART** regimen should be **discussed with the person and individualized** taking into account tolerability, possible adherence issues, as well weighed against potential risk coming from ART exposure or suboptimal pharmacokinetics in pregnancy.
- Pregnant women starting ART should be **monitored monthly or bimonthly** (**depending on adherence and length of virological suppression**) and as close as possible to the predicted delivery date. **HIV-VL should be tested every two months of pregnancy and including 36 weeks of gestation**.

A drug resistance test is recommended in all cases as soon as possible after diagnosis

EACS Guidelines. v.12.1 2024

Recommended antiretroviral regimen for ART-naïve pregnant women

Regimen	Main Requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI (PREFERRED)		
TDF/XTC or TAF/FTC + DTG		I (Tenofovir salts)
2 NRTIs + PI/r		
TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg bid	With food	I (Tenofovir salts) II (DRV dosing) III (COBI boosting)

EACS Guidelines. v.12.1.2024

Alternative antiretroviral regimen for ART-naïve pregnant women

Alternative regimens		
2 NRTIs + INSTI		
TDF/XTC or TAF/FTC + RAL 400 mg bid		I (Tenofovir salts) IV (RAL in pregnancy, bid dosing)
TAF/FTC/BIC qd		I (Tenofovir salts)
ABC/3TC + DTG or ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	V (ABC: HLA-B*57:01, may delay starting ART)
ABC/3TC + RAL 400 mg bid	HLA-B*57:01 negative HBsAg negative	IV (RAL in pregnancy, bid dosing) V (ABC: HLA-B*57:01, may delay starting ART)
2 NRTIs + NNRTI		
ABC/3TC + EFV	HLA-B*57:01 negative HBsAg negative HIV-VL < 100,000 copies/mL At bedtime or 2 hours before dinner	V (ABC: HLA-B*57:01, may delay starting ART) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + EFV or TDF/FTC/EFV	At bedtime or 2 hours before dinner	I (Tenofovir salts) VI (EFV HIV-2 & group O)
TDF/XTC or TAF/FTC + RPV or TDF/FTC/RPV or TAF/FTC/RPV	CD4 count > 200 cells/μL HIV-VL < 100,000 copies/mL Not on gastric pH increasing agents With food	I (Tenofovir salts) VII (RPV exposure during 2nd and 3rd trimester, HIV-2) VIII (Interactions)
2 NRTIs + PI/r		
ABC/3TC + DRV/r 600 mg/100 mg bid	HLA-B*57:01 negative HBsAg negative With food	II (DRV dosing) III (COBI boosting) V (ABC: HLA-B*57:01, may delay starting ART)

EACS Guidelines. v.12.1. 2024

AIDS 2022
29 July – 2 August

Update on Neural Tube Defects with Antiretroviral Exposure in the Tsepamo Study, Botswana

Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

Rebecca Zash,[1,2,3] Lewis B Holmes[4] Modiegi Diseko,[1] Denise L Jacobson,[2] Gloria Katuta Mayondi,[1] Judith Mabuta,[1] Maya Jackson-Gibson,[5] Mompati Mmalane,[1] Tendani Gaolathe[1,6] Shahin Lockman[1,2,7], Joseph Makhema,[1,2] and Roger Shapiro [1,2]

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

[1]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana, [2]Harvard T.H. Chan School of Public Health, Boston, USA, [3]Beth Israel Deaconess Medical Center, Boston, USA, [4]MassGeneral Hospital for Children, Boston, USA, [5]Northwestern University Feinberg School of Medicine, Chicago, USA, [6]University of Botswana, Gaborone, Botswana, [7]Brigham and Women's Hospital, Division of Infectious Disease, Boston, USA

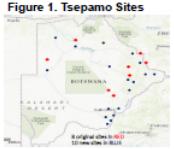
BOTSWANA HARVARD AIDS INSTITUTE PARTNERSHIP FOR HIV RESEARCH AND EDUCATION

BACKGROUND

- Botswana began using Dolutegravir (DTG) as first-line antiretroviral treatment (ART) in 2016. In May 2018, the Tsepamo Study first reported a possible safety signal for neural tube defects (NTDs) associated with DTG exposure at conception.
  - Original signal: 0.94% NTDs for conception DTG (N=426) vs. 0.12% for other ART (N=11,300)
- With additional DTG exposure data, the signal declined.
  - March 2021: 0.15% NTDs for conception DTG (N=5,860) vs. 0.10% (22,475)
- **We now report updated data collected in Tsepamo through March 2022.**

METHODS

Figure 1. Tsepamo Sites



- We conducted birth outcomes surveillance at government hospitals in Botswana, currently covering ~70% of all births in the country (Figure 1)
- Midwives perform surface examinations of all live births and stillbirths and described abnormalities.
- Research assistants photographed major abnormalities after maternal consent, which were reviewed by a birth defects expert blinded to exposures
- Prevalence of NTDs was determined by maternal HIV and antiretroviral exposure status (95%CI by Wilson method) and the primary analysis evaluated prevalence differences by exposure status (95%CI by Newcombe method).

STUDY POPULATION

- Between Aug 15, 2014 and March 31, 2022, 224,251 deliveries occurred at study sites. This analysis includes 223,797 (99.8%) with an evaluable infant surface exam.
  - 9,460 were exposed to DTG from conception
  - 23,664 were exposed to non-DTG ART from conception (14,432 specifically to EFV)
  - 6,551 started DTG during pregnancy
  - 170,723 were born to women without HIV

Figure 2. Trends in NTD Prevalence (and 95% CI) with a) Dolutegravir (DTG) at conception, b) non-DTG ART at conception, c) EFV at conception and d) women without HIV March 2021-March 2022

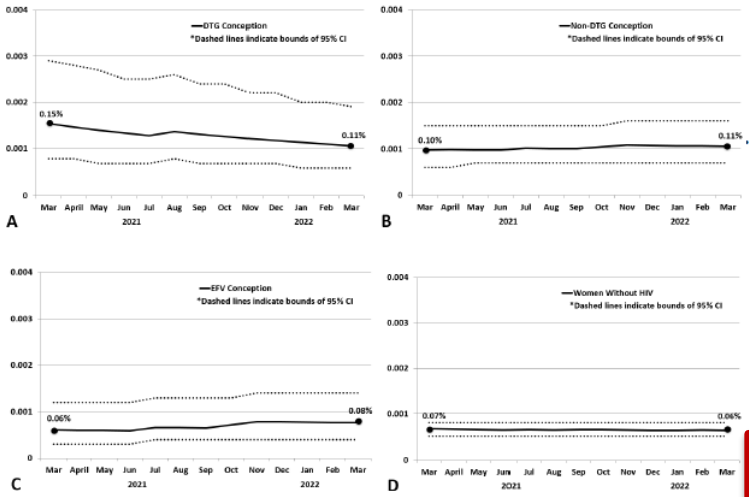


Table 1. Prevalence Difference of Neural Tube Defects by ARV and HIV Exposure Categories

Exposure group vs. Comparison group	Prevalence Difference (%) (95% CI)
DTG at conception vs. Non-DTG at conception	0.00 (-0.07, 0.10)
DTG at conception vs. EFV at conception	0.03 (-0.05, 0.12)
DTG at conception vs. DTG started in pregnancy	0.04 (-0.06, 0.14)
DTG at conception vs. Women without HIV	0.04 (-0.01, 0.13)

RESULTS

- **Since March 2021 (last Tsepamo update) (Figure 2)**
  - 32,819 additional births were recorded, including 3,600 additional DTG conception exposures.
  - 16 additional NTDs were identified:
    - 1 with DTG-conception exposure
    - 3 with non-DTG conception exposure
    - 1 with DTG started during pregnancy
    - 11 among women without HIV
  - The additional NTD with DTG-conception exposure was anencephaly (no photo)
- **Since August 2014 (entire study)**
  - **In total:** 156 (0.07%, 95% CI 0.06%, 0.08%) NTDs identified (100 with photo, 56 by description only).
  - **DTG at conception:** 10 NTDs among 9,460 exposures (0.11%; 95%CI 0.06%, 0.19%)
  - **Non-DTG ART at conception:** 25 NTDs among 23,664 exposures (0.11%; 95%CI 0.07%, 0.16%)
    - **EFV at conception:** 11 NTDs among 14,432 exposures (0.08%; 95%CI 0.04%, 0.14%)
  - **DTG during pregnancy:** 4 NTDs among 6,551 exposures (0.06%; 95%CI 0.02%, 0.16%)
  - **Women without HIV:** 108 NTDs among 170,723 exposures (0.07%; 95%CI 0.05, 0.08%)

CONCLUSIONS

- The prevalence of NTDs among infants born to women on dolutegravir at conception has declined slightly to 0.11% and does not substantially differ from other exposure groups.
- These data support existing WHO guidelines that recommend DTG as first-line for use in all adults, regardless of reproductive potential

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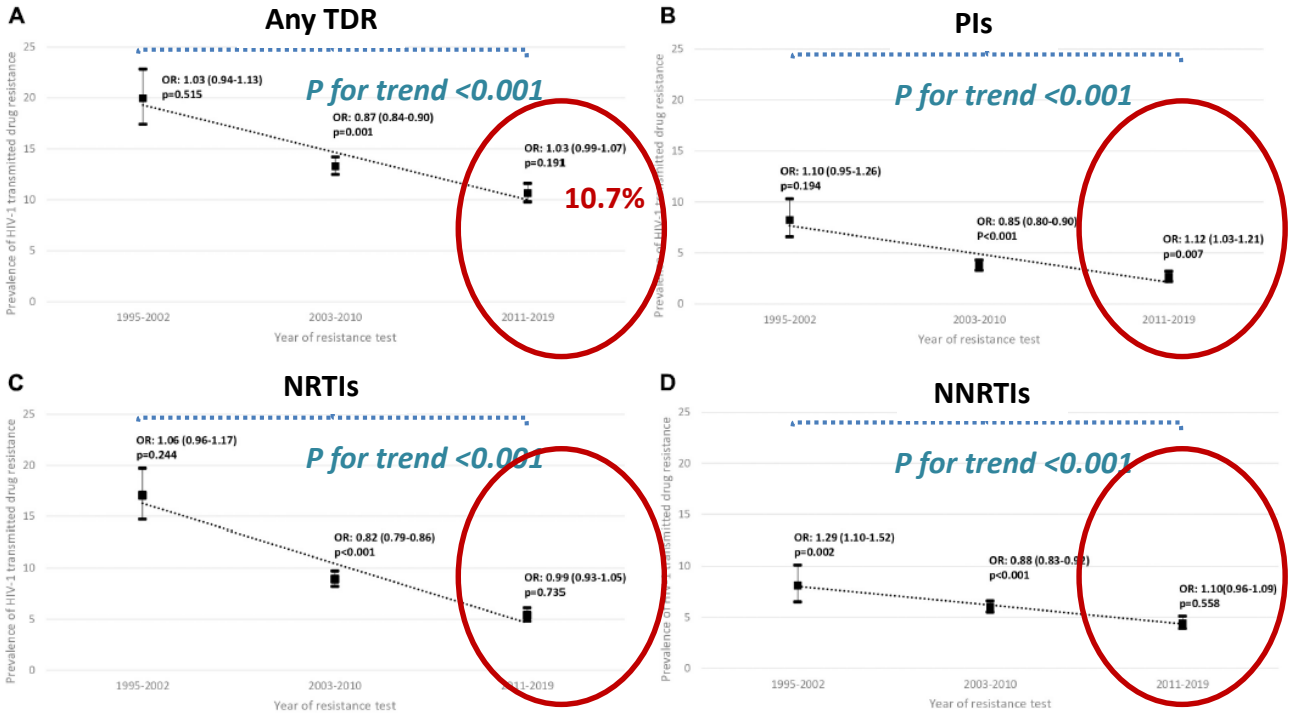
Drug resistance testing is recommended…

For Initial Treatment of HIV

- HIV drug-resistance testing is recommended at entry into care for people with HIV to guide the selection of the initial antiretroviral (ARV) regimen **(AII).** If antiretroviral therapy (ART) is deferred, repeat testing may be considered at the time of ART initiation **(CIII).**
- The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends genotypic, rather than phenotypic, testing as the preferred resistance testing to guide therapy in ARV-naive people **(AIII).**
- In people with early (acute and recent) HIV infection, in pregnant people with HIV, or in people who will initiate ART on the day of or soon after HIV diagnosis, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported **(AIII).**
- Standard genotypic drug-resistance testing in ARV-naive people involves testing for mutations in the reverse transcriptase and protease genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is suspected, if the person has ever used long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis, or if the person has ever received an INSTI-based regimen for post-exposure prophylaxis, providers should ensure that genotypic resistance testing also includes the integrase gene **(AIII).**

DHHS Guidelines. 2024.

Transmitted drug resistance in Europe presented decreasing trends from 1995 to 2019

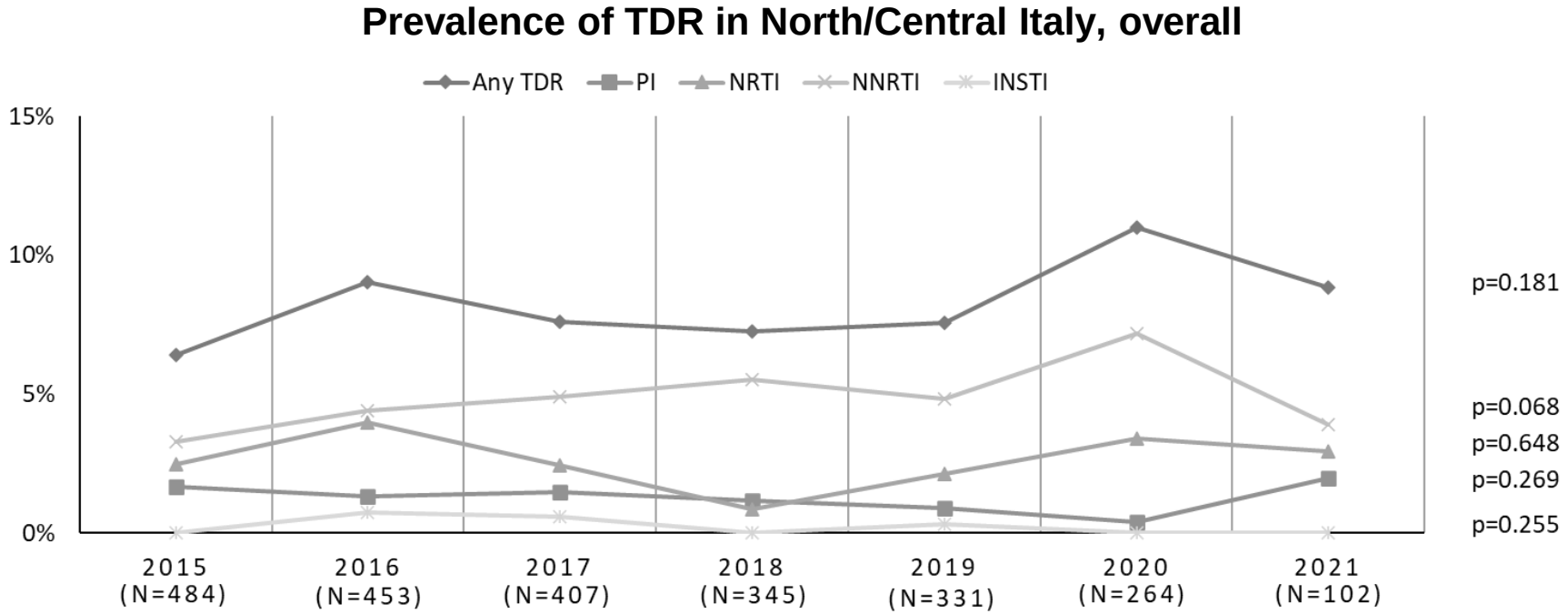


Analysis on 11,581 ART-naïve PWH

FIGURE 1 | Proportion of **(A)** overall transmitted drug resistance (TDR), **(B)** of protease inhibitors (PIs), **(C)** of nucleoside reverse transcriptase inhibitor (NRTIs) and **(D)** of non-nucleoside reverse transcriptase inhibitor (NNRTIs) in sequences from drug-naïve patients between three periods 1995–2002, 2003–2010, and 2011–2019. OR, Odds Ratio; *p*, *p*-value.

Miranda et al. Frontiers in Microbiol 2022

No significant changes in the prevalence of TDR to any class were found over 2015-2021 on 2,386 ART-naïve PWH



Overall TDR prevalence: 8.0%

3TC/FTC mutation **M184V** was negligible (n=9, 0.4%)

Fabeni et al., 2024, J Antimicrob Chemother https://doi.org/10.1093/jac/dkae189

Transmission of HIV with integrase inhibitor (INI) resistance is so far a rare event.

Fabeni et al., JAC 2024; Matsuda et al., AIDS Res Hum Retroviruses 2024; De Salazar et al. CID 2023; Muccini et al., JAC 2023; Šablinskaja et al., J Glob Antimicrob Resist. 2023; Rossetti et al., JAC 2021; McClung et al., CID 2021; Baxter et al., HIV Med 2021; A de Salazar et al., Virtual meeting on HIV Drug Therapy 2020 (abstract); Mbisa et al., JAC 2020; Casadellà et al., JAC 2020; Mazzuti L et al., J Glob Antimicrob Resist 2019; Armenia et al., CROI 2019 (abstract 2302); Günthard et al., CID 2018; Hernandez AL, et al. CROI 2017 (Abstract 478); Scherrer AU, et al. J Infect Dis. 2016; Casadellà M, et al. JAC 2015.

HIV Transmitted Drug Resistance in 2705 newly diagnosed individuals naïve to ART, from the MEDITRES Consortium, 2018-2021

The prevalence of **NRTI SDRMs** was **5.77%**, while for **INSTI** it was **0.30%**

SDRM INSTI	n, (%)
T66A	1 (0.04%)
T66I	1 (0.04%)
E92Q	1 (0.04%)
E138T	1 (0.04%)
E138K	1 (0.04%)
Y143R	1 (0.04%)
S147G	1 (0.04%)
R263K	1 (0.04%)
Total	**8 (0.30%)**

SDRM NRTI	n, (%)
M184V	23 (0.85%)
M184I	5 (0.18%)
K65R/N	3 (0.11%)
K70E	2 (0.07%)
L74V/I	5 (0.18%)
V75M	4 (0.15%)
Y115F	1 (0.04%)
T69D	10 (0.37%)
M41L	28 (1.04%)
D67N/G	9 (0.33%)
K70R	2 (0.07%)
L210W	10 (0.37%)
T215Y/F	4 (0.15%)
T215D/S/E/C/V	24 (0.89%)
K219E/Q/N	11 (0.41%)
K219R	15 (0.55%)
Total	**156 (5.77%)**

Countries involved: Italy, Spain, Portugal, France, Greece

De Salazar et al. CID 2023

Clinically relevant resistance defined as any resistance level for Stanford interpretation >= 3

Integrase Strand Transfer Inhibitor	n (%)	95%CI
Raltegravir	62 (2.29)	1.76%–2.93%
Elvitegravir	62 (2.29)	1.76%–2.93%
Dolutegravir	4 (0.15)	.04%–.38%
Bictegravir	4 (0.15)	.04%–0.38%
Total	63 (2.33)	1.80%–2.97%
Nucleoside/Nucleotide Reverse Transcriptase Inhibitor		
Tenofovir alafenamide	24 (0.89)	.57%–1.32%
Abacavir	47 (1.74)	1.28%–2.31%
Lamivudine/Emtricitabine	29 (1.07)	.72%–1.53%
Total	47 (1.74)	1.28%–2.31%

Countries involved: Italy, Spain, Portugal, France, Greece

De Salazar et al. CID 2023

INSTI Baseline Resistance Substitutions: No Impact on Virologic Suppression in Treatment-Naive Patients

- High viral suppression rates with first-line BIC/FTC/TAF and DTG + FTC/TAF in GS-1489 and GS-1490
- Preexisting INSTI resistance present in 1.3% of patients in both studies
  - T97A was the most common INSTI resistance mutation
- All patients with transmitted INSTI resistance achieved viral suppression at Wk 48

HIV-1 RNA <50 c/mL at Wk 48 by INSTI Resistance, n/N (%)	BIC/FTC/TAF (n = 634)	DTG + FTC/TAF (n = 325)
INSTI mutation		
▪ Any	7/7 (100)	6/6 (100)
▪ None	568/625 (90.9)	295/318 (92.8)
P value	1.0	1.0
T97A		
▪ Yes	6/6 (100)	6/6 (100)
▪ No	569/626 (90.9)	295/318 (92.8)
P value	1.0	1.0

Acosta. Antimicrob Agents Chemotherapy. 2019;63:e02533.

Data from Switch Studies in Patients With Baseline Resistance

DAWNING[1]

- Response rates consistently high with **DTG + 2 NRTIs** regardless of baseline NRTI RAMs to the second-line NRTI
  - HIV-1 RNA <50 copies/mL at Wk 48
    - In patients with BL M184V/I ± other NRTI RAMs receiving 3TC or FTC: 85%
    - In patients with K65R receiving TDF: 86%
    - In patients with ≥1 TAM receiving ZDV: 86%

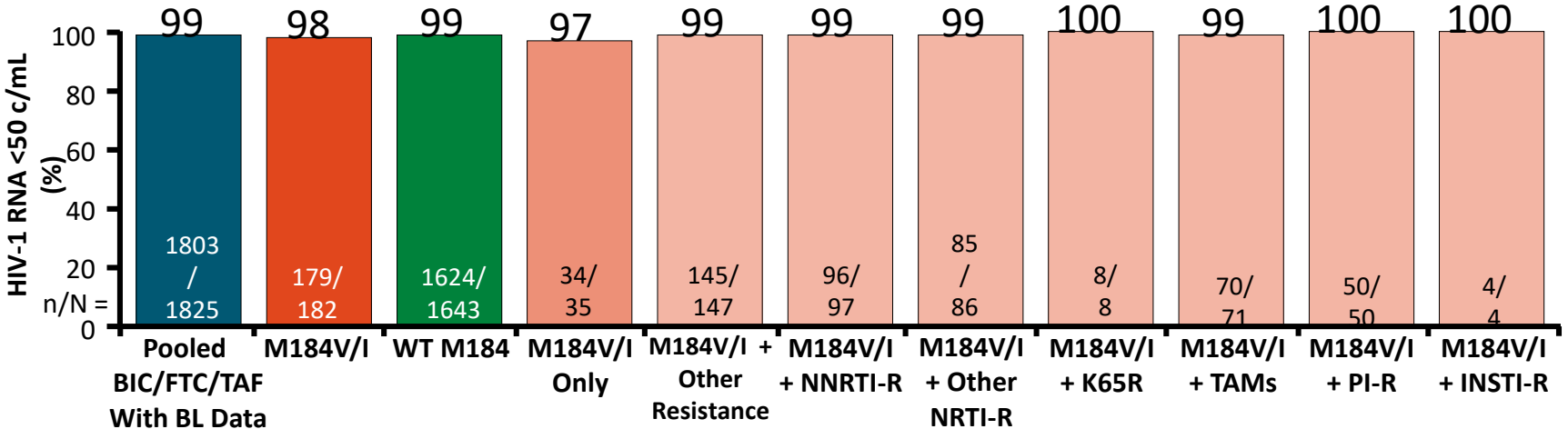
NADIA[2,3]

- Response rates consistently high with both **DTG and DRV/RTV + 2 NRTIs** regardless of baseline NRTI RAMs
  - HIV-1 RNA <400 copies/mL at Wk 48
    - In patients with BL M184V/I
      - 94% receiving TDF
      - 92% receiving ZDV
    - In patients with BL K65R/N
      - 94% receiving TDF
      - 96% receiving ZDV

1. Brown. CROI 2019. Abstr 144. 2. Paton. CROI 2021. Abstr 94LB. 3. Paton. NEJM. 2021;385:330.

Switch to BIC/FTC/TAF: Effect of M184V/I on Virologic Efficacy

- Pooled analysis of 6 clinical trials in which **virologically suppressed patients switched to BIC/FTC/TAF** (N = 2034)
  - HIV-1 RNA ≥50 c/mL at last visit in 3 patients with M184V/I; HIV-1 RNA 2860 c/mL for 1 patient (poor adherence, undetectable plasma BIC but no emergent resistance) and HIV-1 RNA <100 c/mL for 2 patients (resuppressed with BIC/FTC/TAF or ATV/RTV + FTC/TDF)



PE Sax, AIDS, 2022

Key Points

- Rapid ART is important
  - for reducing community transmission
  - for upholding equity
- Guidelines agree that ART should be initiated as soon as possible when indicated
- ART regimens with high barriers to resistance are referred for rapid initiation
  - BIC/FTC/TAF, boosted DRV + (FTC or 3TC)/(TAF or TDF), or DTG + (FTC or 3TC)/(TAF or TDF)
  - There are data to support the use of these regimens even with common baseline resistance mutations
- There are data for the use of DTG/3TC for rapid initiation
- Warning in PREP failure

Grazie per l'attenzione!