# Strategie di semplificazione

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# Disclosures

**Grants for educational activities**

- Janssen-Cilag
- Merck Sharp and Dohme
- ViiV Healthcare
- Gilead

**Personal fees for advisory boards and speakers bureau**

- Janssen-Cilag
- Merck Sharp and Dohme
- ViiV Healthcare
- Gilead

# Switch after virological suppression: rationale and strategies

**Clinicians should always review possible adverse events or tolerability issues with current antiretroviral regimens. Just because the viremia is suppressed it should not be assumed that the person is well adapted and tolerating the current regimen**

### Definition of virologically suppressed

Clinical trials exploring switching strategies have generally defined suppression as an HIV-VL < 50 copies/mL for at least 6 months

### Indications

1. **Documented toxicity** caused by one or more of the antiretrovirals included in the regimen, see Adverse Effects of ARVs and Drug Classes
2. **Prevention of long-term toxicity**, see Adverse Effects of ARVs and Drug Classes. This may include person's concerns about safety
3. **Avoidance of drug-drug interactions,** page 26. This includes ART switch when starting HCV treatment to avoid DDIs, see Drug-drug Interactions between Viral Hepatitis Drugs and ARVs
4. **Planned pregnancy or women wishing to conceive,** see Treatmen of Pregnant Women Living with HIV or Women Considering Pregnanc
5. **Ageing and/or comorbidity** with a possible negative impact of drug( in current regimen, e.g. on CVD risk, metabolic parameters
6. **Simplification**: to reduce pill burden, adjust food restrictions, improve adherence and reduce monitoring needs
7. **Protection from HBV** infection or reactivation by including tenofovir i the regimen
8. **Regimen fortification**: Increasing the barrier to resistance of a regime in order to prevent VF (e.g. in persons with reduced adherence)
9. **Cost reduction:** switching to the generic form of their current regime if available

3. Switches within the same drug class (i.e. TDF/FTC -> TAF/FTC, EFV -> DOR or RPV) are usually virologically safe if equal potency and in the absence of resistance
4. Cross-class switches of single drugs with the same barrier to resistance (for example EFV to RAL) are usually virologically safe in the absence of resistance to the new compound
5. In case of prior virologic failures, with or without evidence of resistance, switches have to be planned especially carefully when they result in a lower barrier to resistance of the regimen. A PI/b may only be switched to an NNRTI, INSTIs RAL if full activity of the 2 NRTIs in the new regimen can be assumed based on resistance data, ARV history and HIV-VL results before switching (see 2.) Due to the higher barrier to resistance of DTG and BIC, it is currently unclear if a switch to DTG- or BIC-based regimens also requires full activity of 2 NRTIs in the combination
6. Before switching, remaining treatment options in case of potential virological failure of the new regimen should be taken into consideration. This requires knowledge about the resistance selection profile of the switch regimen. Especially, when reducing the number of drugs in a regimen or its barrier to resistance, the chances of composing a fully suppressive regimen after potential failure following switch should be considered
7. Proviral DNA genotyping may be useful in persons with multiple virological failures, unavailable resistance history or low-level viremia at the time of switch. Results ought to be taken cautiously as proviral DNA genotype may not detect previous resistance mutations and can also detect clinically irrelevant mutations. Therefore, routine proviral DNA genotyping is currently not recommended

### Dual therapies

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is
- a) no historical resistance and
- b) HBV immunity with anti-HBs antibodies (if non-immune provide HBV Vaccination, if isolated HBc antibodies see the section on Treatment and Monitoring of Persons with HBV/HIV Co-infection for details)

**Oral dual therapies supported by large randomized clinical trials or meta-analyses:**
- DTG + RPV
- XTC + DTG
- XTC + DRV/b

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

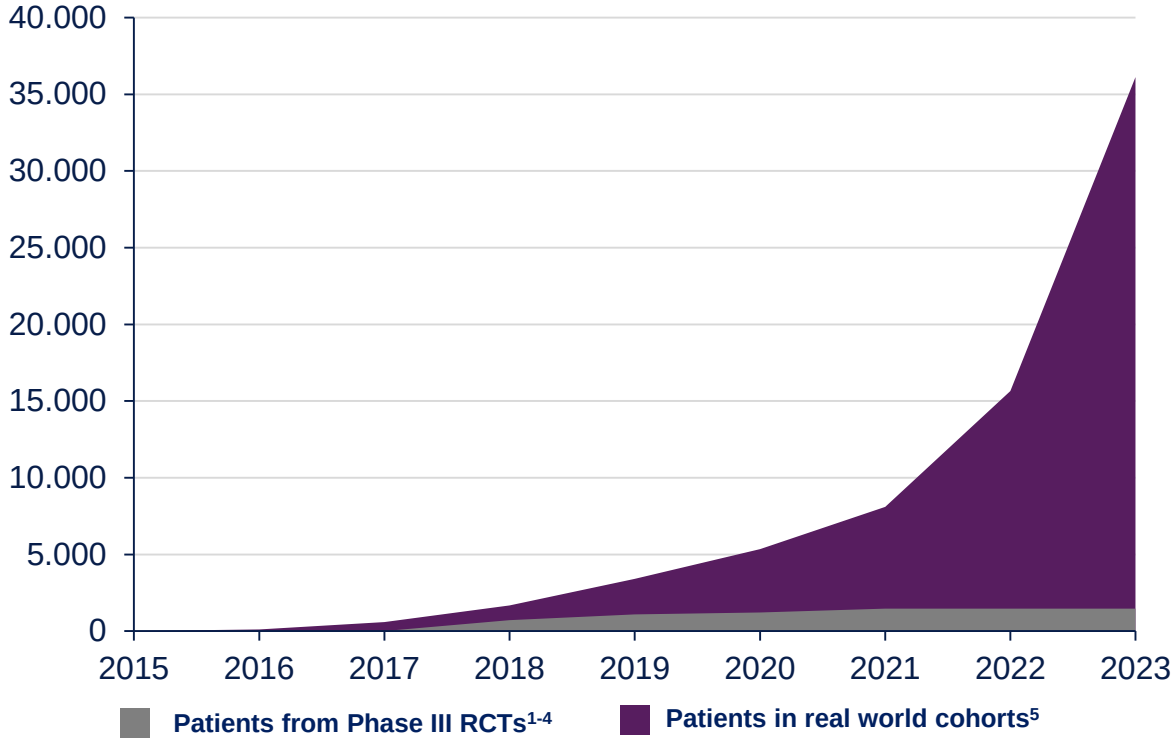
**Long-acting intramuscular dual therapy CAB + RPV**

- The use of oral lead-in (1 month) is optional
- Injections are administered every 2 months. In case of bridging, see the section on Drug-Drug Interactions after Oral and Intramuscular Administration of CAB and RPV

| Initiation phase (start on day of last oral pills) | Continuation phase |
|---|---|
| Day 0: CAB 600 mg/ RPV 900 mg<br>Month 1: CAB 600 mg/ RPV 900 mg | From month 2 onwards:<br>CAB 600 mg/ RPV 900 mg every 2 months |

The following baseline factors, when combined, are associated with risk of virologic failure and resistance:
- Archived RPV-associated mutations
- HIV subtype A6/A1
- BMI ≥ 30 kg/m²

# REAL WORLD DATA ON DTG/3TC HAS GROWN RAPIDLY IN RECENT YEARS[5]




**As of October 2023**

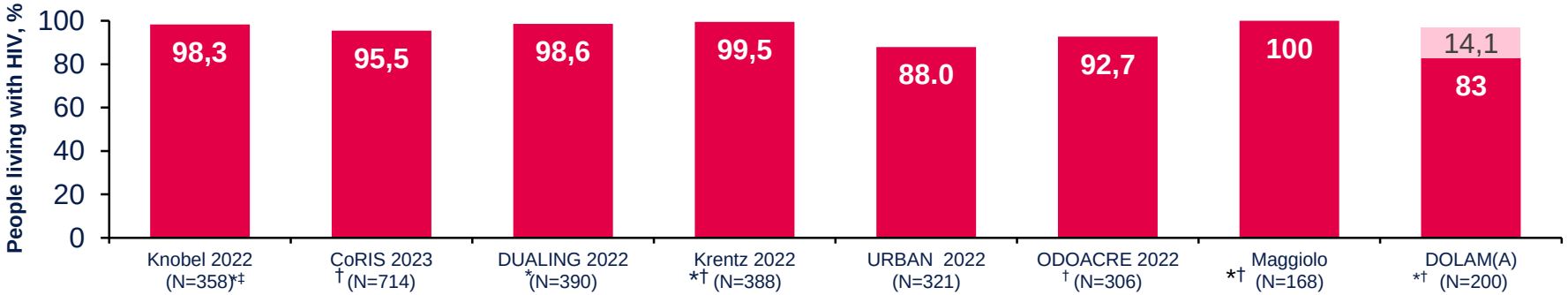
**>36.000**

**Treatment naïve & switch patients have received DTG/3TC in real world studies[5]**

**1.** Cahn P et al. AIDS. 2022;36(1):39-48. **2.** Rolle CP et al. Open Forum Infectious Diseases. 2023. Epub ahead of print. **3.** Osiyemi O *et al.*Clin Infect Dis. 2022;75(6):975-986 **4.** Llibre JM *et al.* Clin Infect Dis. 2023;76(4):720-729. **5.** Lertang E, *et al*. Poster eP.A.050. EACS 2023.Disponibile: https://eposters-eacs2023.medicalcongress.online/mediatheque/media.aspx?mediaId=180790&channel=109239 Ultimo accesso novembre 2023.

# Effectiveness outcomes reported in treatment-experienced people who switched to DTG + 3TC in real-world studies with N≥300

## Reported effectiveness outcomes vary between studies (stated below chart)




| | Knobel 2022 (N=358)*‡ | CoRIS 2023 † (N=714) | DUALING 2022 *(N=390) | Krentz 2022 *† (N=388) | URBAN 2022 (N=321) † | ODOACRE 2022 † (N=306) | *† Maggiolo (N=168) | DOLAM(A) *† (N=200) |
|---|---|---|---|---|---|---|---|---|
| **Timepoint** | Median FU 41.9 weeks[1] | Week 48[2] | 1 year[3] | 1 year[4] | 2 years[5] | 660.3 PYFU up to Week 240[6] | 5 years[8] | Week 48[9] |
| **Effectiveness outcome** | VL <50 c/mL | VL <50 c/mL | VL <50 c/mL (on treatment) | VL <400 c/mL (MEX) | Achieved/ maintained viral suppression§ | Estimated probability of maintaining viral suppression‖ | Remained free of VF (MEX)‖ | VL <50 c/mL (PP, ITT) |

**High rates of virologic effectiveness were observed across real-world cohorts, consistent with the Phase III TANGO and SALSA trials[12–15]**

TANGO SALSA

*People viraemic at BL: BREACH n=20; Cheng n=6; Martínez-Serra n=34; SPADE n=89; URBAN n=11
†People excluded due to missing data or not being treated per protocol: CoRIS n=742; Martínez-Serra n=507; DUALING n=28; Krentz n=3; SPADE n=607; URBAN n=21
‡N=697 treatment-experienced people at BL, n at Week 48 NR
§Definitions of VF: CSLHIV, confirmed HIV-1 RNA >50 c/mL or single HIV-1 RNA >50 c/mL followed by treatment modification or single HIV-1 RNA >1,000 c/mL; ODOACRE, confirmed HIV-1 RNA ≥50 c/mL or single HIV-1 RNA ≥1,000 c/mL
‖ viral suppression in URBAN was defined as HIV-1 RNA <50 c/mL in visit window 21–27 months or 50–200 c/mL with subsequent HIV-1 RNA <50 c/mL



1.Knobel H, et al. AIDS 2022. Poster EPB168, 2. Suárez-García I, et al. J Antimicrob Chemother 2023;78:1423–32 (and suppl. appendix), 3. Vasylyev M, et al. HIV Glasgow 2022. Poster P080, 4. Krentz HB, et al. AIDS Patient Care STDs 2022;36:1–7, 5. Beer D, et al. HIV Glasgow 2022. Poster 117, 6. Ciccullo A, et al. JAC. 2022 Dec 23;78(1):117-121, 8. . Maggiolo F, et al. IAS 2021. Poster PEB179, 9. Liano P, et al. EACS 2021. Poster PE2/38

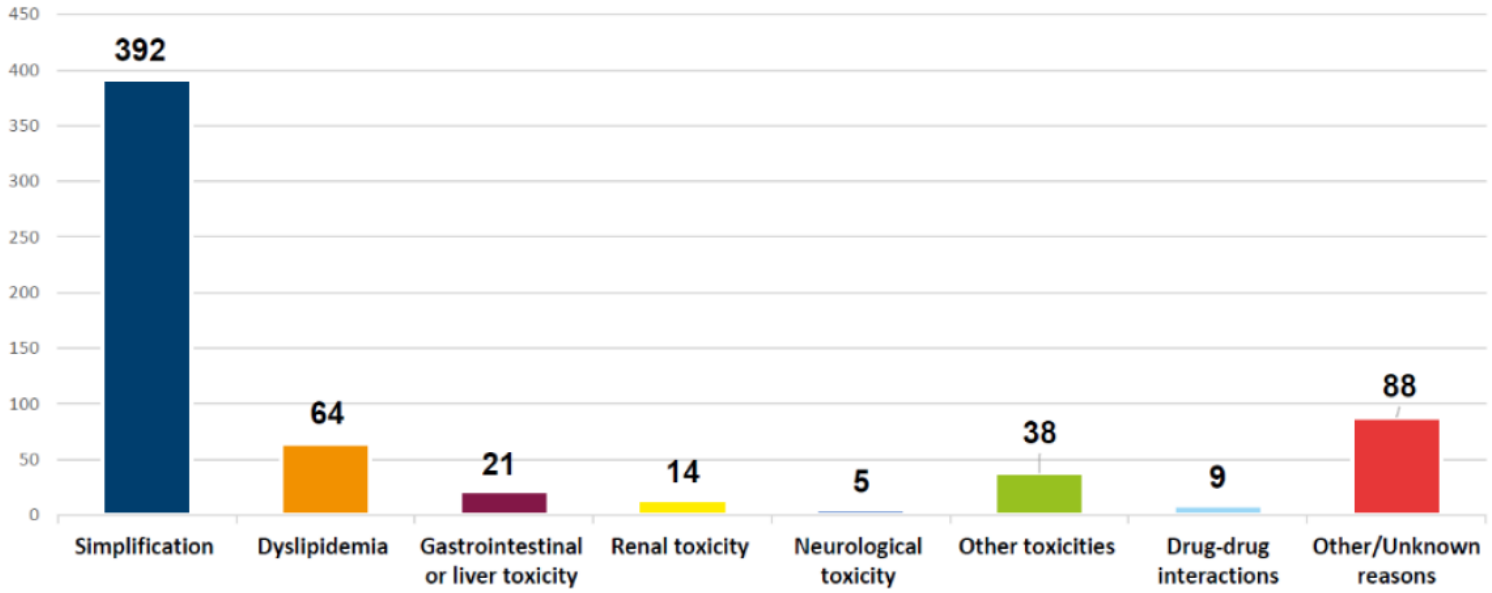
# ODOACRE: Real-world Italian Cohort

**Study design:**
Retrospective, multicenter, Italian cohort of 631 ART-experienced PLWH starting DTG/3TC

| Variables (N=631) | |
|---|---|
| **Age (years), Median (IQR)** | 51.1 (42.6 – 57.6) |
| **Male, n (%)** | 446 (70.7) |
| **Risk factor for HIV infection, n (%):** | |
| - Heterosexual | 261 (41.4) |
| - MSM | 264 (41.8) |
| - IDU | 45 (7.1) |
| - Others | 61 (9.7) |
| **Anti-HCV antibodies positive, n (%)** | 74 (11.8) |
| **Time from HIV diagnosis (years), Median (IQR)** | 12.7 (6.5 – 19.7) |
| **CDC stage C, n (%)** | 144 (22.8) |
| **Time on antiretroviral therapy (years), Median (IQR)** | 10.2 (5.6 – 11.1) |
| **Nadir of CD4+ (cell/µL), Median (IQR)** | 220 (82 - 331) |
| **Zenith HIV-RNA (log copies/mL), Median (IQR)** | 4.91 (4.34 – 5.42) |
| **Zenith HIV-RNA > 500.000 copies/mL, n (%)** | 63 (10.9) |
| **Previous virological failure, n (%)** | 244 (38.7) |
| **CD4+ count (cell/µL), Median (IQR)** | 665 (513 - 841) |
| **Time of virological suppression (months), Median (IQR)** | 92 (48 – 141) |
| **Previous ARV regimen:** | |
| - 2NRTIs + INI | 266 (42.3) |
| - 2NTRIs + NNRTI | 170 (27.0) |
| - 2NRTIs + PI | 29 (4.6) |
| - 3TC + bPI | 135 (21.5) |
| - Other | 29 (4.6) |

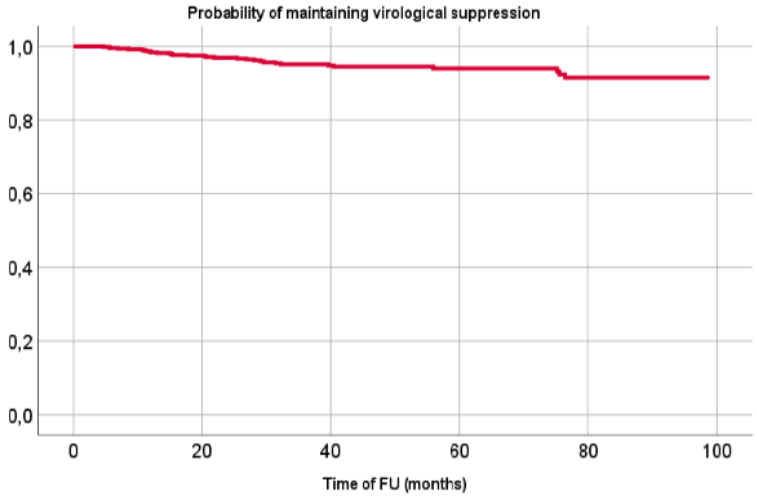
Baldin et al. ICAR 2023; Bari, Italy. oral communication OC 65.
Baldin et al. Submitted AIDS 2024

# ODOACRE: Results 1

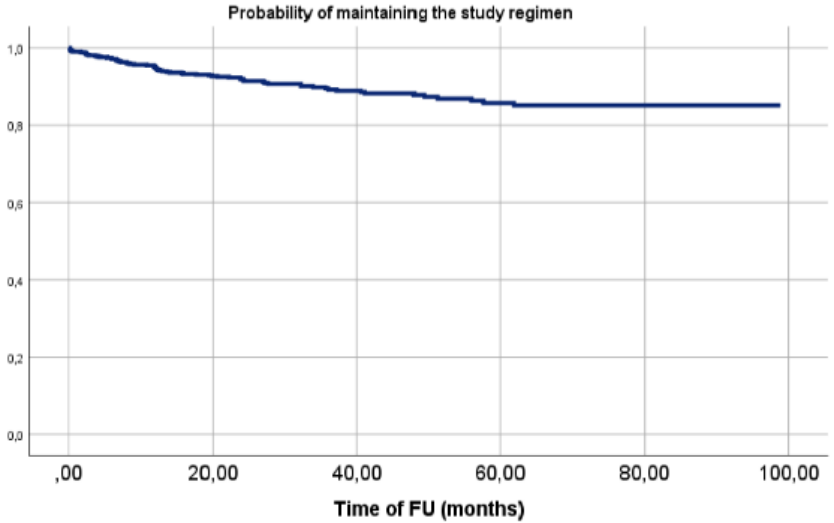


# ODOACRE: Results 2

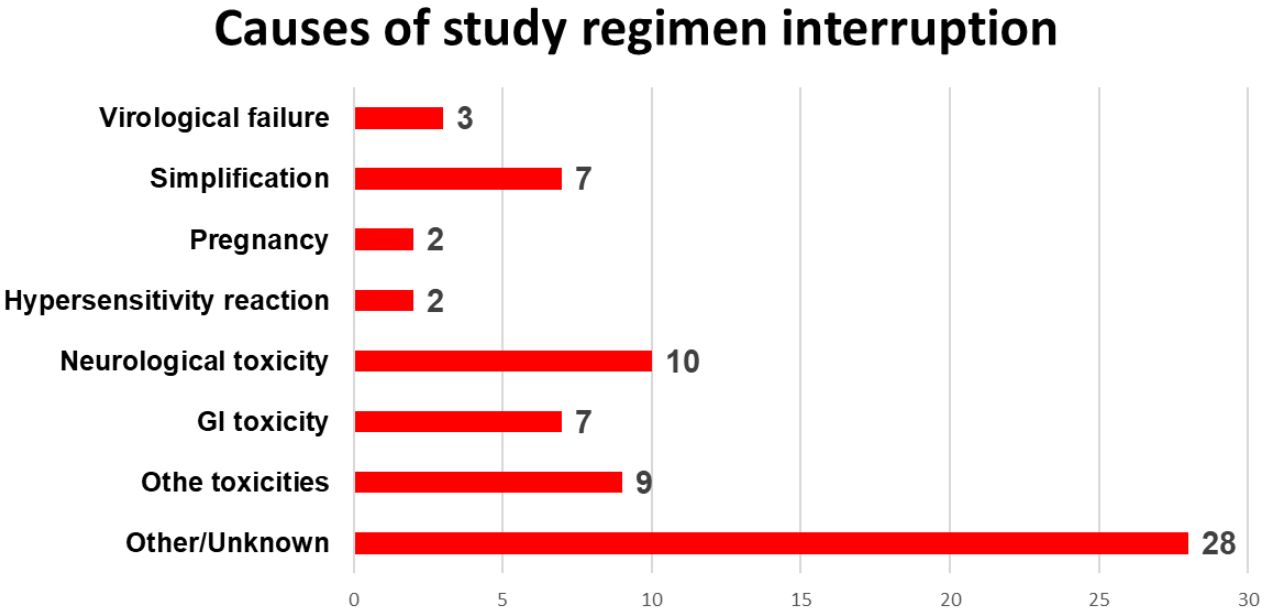
- Durante 2291.82 anni-paziente di follow-up, sono stati osservati **31** fallimenti virologici (tasso di 1.3 VF per 100 PYFU)
- Probabilità stimate di mantenere la soppressione virologica:
  - 48 mesi (4 anni)= **95.1%** (95%CI 92.0-96.2)
  - 96 mesi (8 anni) = **91.5%** (95%CI 87.1-94.4)




- Durante 2111,13 anni-paziente di follow-up, sono stati osservate **67** interruzioni del trattamento (tasso di 3.2 TD per 100 PYFU)
- Probabilità stimate di mantenere il regime dello studio:
  - 48 mesi (4 anni)= **87.8%** (95%CI 84.5-90.5)
  - 96 mesi (8 anni) = **85.1%**(95%CI 81.0-88.5)



# ODOACRE: Results 3



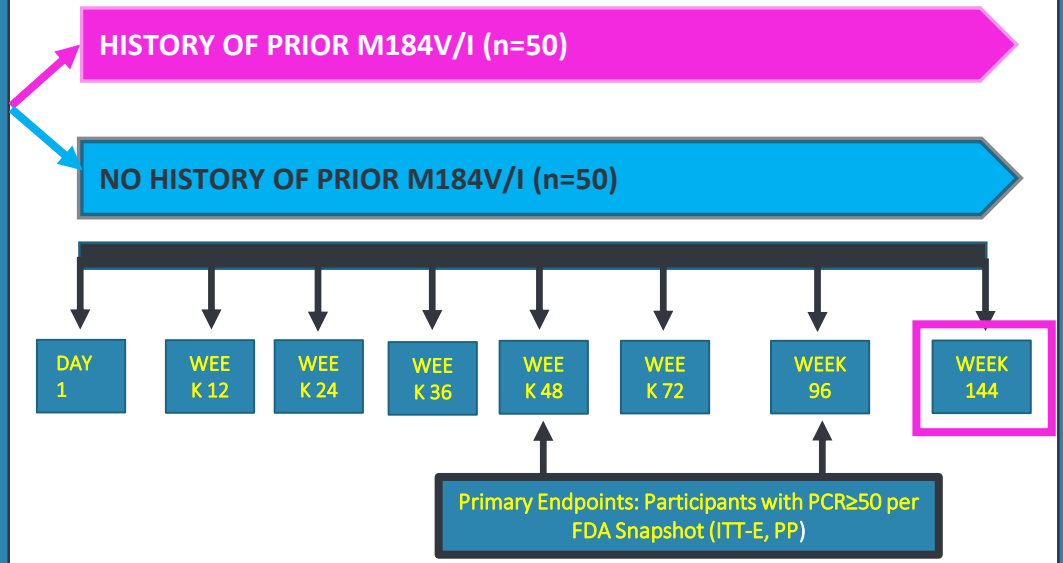

**The study shows that dolutegravir+lamivudine is an effective and safe switch strategy in clinical practice, with a low cumulative incidence of VF and TD, even in the long term (8 years of FU).**

# SOLAR-3D Study

ELIGIBILITY CRITERIA:

- HIV+ Adults aged ≥18
- HIV-1 RNA <50c/mL for ≥6mos
- Any stable 2-/3-/4-drug ART for ≥6mos
- **Prior virologic failure** (≥2 prior ART with at least 1 of following: failure to attain PCR<50, confirmed rebound PCR>200, documented genotypic/ phenotypic resistance)
- **No exclusion for prior INSTI, any CD4, prior NRTI mutations, or M184V/I or K65R in BL Proviral DNA NGS (above a 10% threshold)**
- COVID Window +/- 1mo.

**SOLAR-3D:**
Prospective, open-label, comparative, 96-week study, [144-week extension] (n=100)




Individuals were consecutively consented and enrolled during regularly scheduled office appointments from 5/2/2019 through 6/16/2020

PRIMARY ENDPOINTS:

- Proportion of pts with PCR≥50 at Wks 48 & 96 (FDA Snapshot, ITT-E, Per Protocol)

SECONDARY ENDPOINTS:

- PCR<50 at Wks 48 & 96 (FDA Snapshot, ITT-E and Per Protocol)
- Discontinuations due to CVF (PCR≥50 followed by PCR>200)

Blick et al. AIDS 2024; Munich, Germany. Oral presentation OAX0903LB.

# Baseline Characteristics

| Baseline Characteristic | All Patients (n = 100) | Historical M184V/I Resistance (n = 50) | No Historical M184V/I Resistance (n = 50) | *P* Value |
|---|---|---|---|---|
| Median Age, yrs (IQR) | 58 (51-64) | 61 (56-66) | 55 (47-61) | <0.001 |
| Cis-/Trans-Gender Female, n (%) | 15 (15) | 11 (22) | 4 (8) | 0.050 |
| Median Time Since HIV Diagnosis, yrs (IQR) | 25.3 (15.0-29.5) | 28.4 (25.1-30.0) | 15.5 (9.8-26.7) | <0.001 |
| Median CD4 Nadir cell/mm3 (IQR) | 190 (64-278) | 160 (45-225) | 225 (88-359) | 0.006 |
| History CD4<200, n (%) | 53 (53) | 33 (66) | 20 (40) | 0.009 |
| Median ART Duration, yrs(IQR) | 22.3 (14.3-25.7) | 24.6 (22.0-28.1) | 15.2 (8.8-22.6) | <0.001 |
| Median Previous ART regimens, n(IQR) | 7 (4-10) | 9 (7-13) | 4 (2-5) | <0.001 |
| Median Duration of HIV-RNA suppression, yrs (IQR) | 11.8 (8.2-14.6) | 12.8 (10.2-14.4) | 8.9 (4.4-14.7) | 0.019 |

There were no significant differences observed for Age at time of HIV diagnosis, Race, HBV/HCV, Median highest PCR or History PCR>100,000c/mL.

Blick et al. AIDS 2024; Munich, Germany. Oral presentation OAX0903LB.

# Switch Characteristics

| Switch Characteristic | All Patients (N = 100) | Historical M184V/I Resistance (n = 50) | No Historical M184V/I Resistance (n = 50) | *P* Value |
|---|---|---|---|---|
| On 3TC/FTC, n (%) | 73 (73) | 34 (68) | 39 (78) | 0.260 |
| Median Time on DTG/3TC, weeks (IQR) | **137.8 (133-151)** | **137.4 (133-151)** | **138.3 (132-151)** | 0.747 |
| CD4 at Switch, Median (IQR) | | | | |
| • CD4% | 30 (25-39) | 27 (24-37) | 32 (27-39) | 0.136 |
| • CD4 abs count, cells/mm# | 610 (425-781) | 617 (412-758) | 593 (434-812) | 0.677 |
| • CD4<200, n (%) | 1 (1) | 1 (2) | 0 | 0.315 |
| • CD4<350, n (%) | 10 (10) | 7 (14) | 3 (6) | 0.182 |
| PCR at Switch, Median (IQR) | | | | |
| • Copies/mL | 1 (1-19) | 1 (1-19) | 1 (1-19) | 0.335 |
| • $Log_{10}$ | 0 (0-1.3) | 0 (0-1.3) | 0 (0-1.3) | 0.806 |
| • PCR>50, n (%) | 2 (2) | 1 (2)[§] | 1(2)[†] | 1.000 |
| • PCR, TND, n (%) | 58 (58) | 28 (56) | 30 (60) | 0.685 |

[§]1 pt with a screening PCR<50 was PCR 73 c/mL at BL. [†]1 pt with screening PCR<50 was PCR 4150 c/mL at BL.

Blick et al. AIDS 2024; Munich, Germany. Oral presentation OAX0903LB.

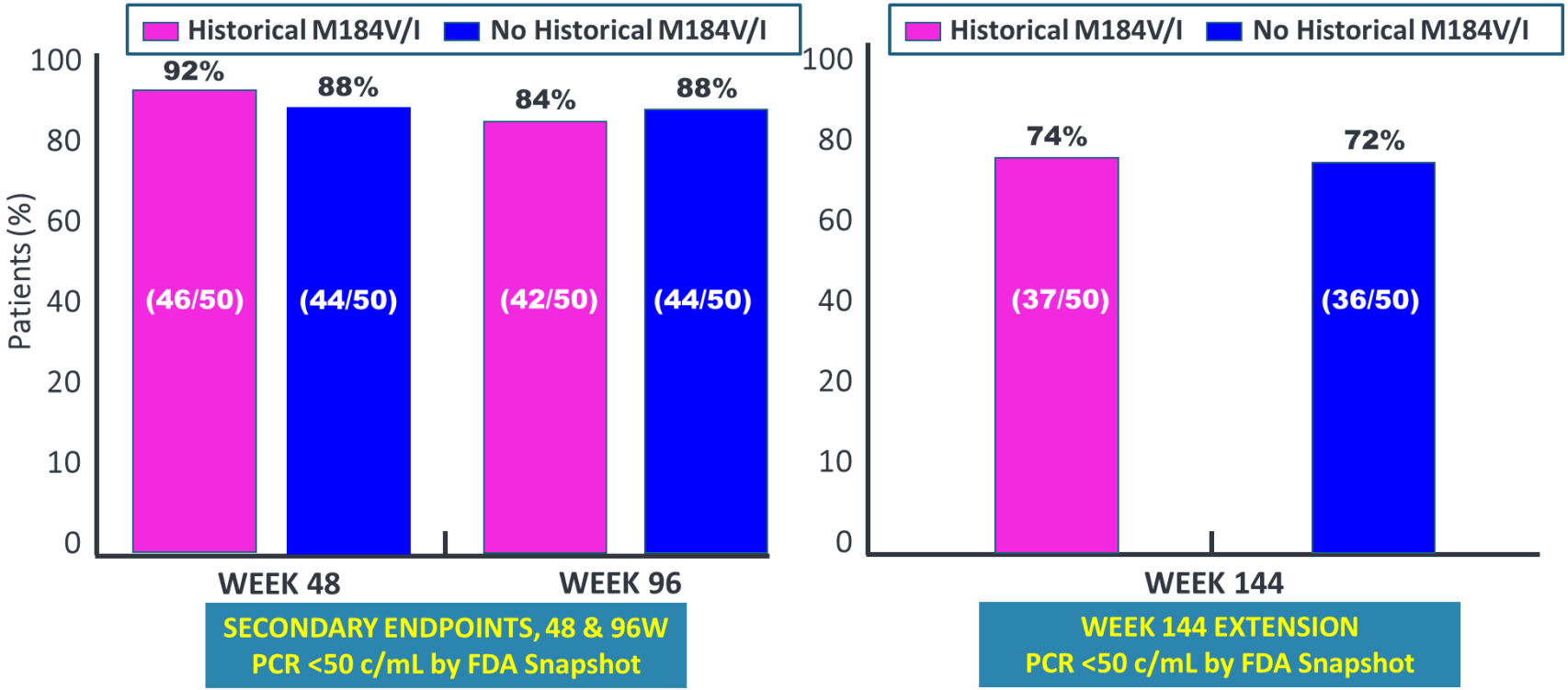
# Baseline ART and Proviral Mutations

| Baseline ART | All Patients (n=100) | Historical M184V/I (n=50) | No Historical M184V/I (n=50) |
|---|---|---|---|
| ART Regimen, n (%): | | | |
| • 2 NRTIs + INSTI: | 58 (58) | 30 (60) | 28 (56) |
| ❖ TAF/FTC/BTG | 4 (4) | 3 (6) | 1 (2) |
| ❖ ABC/3TC/DTG | 51 (51) | 26 (52) | 25 (50) |
| ❖ TDF or TAF/FTC + DTG | 3 (3) | 1 (2) | 2 (4) |
| • 2DR (NNRTI + INSTI): | | | |
| ❖ RPV/DTG | 21 (21) | 12 (24) | 9 (18) |
| • 2 NRTIs + boosted INSTI: | | | |
| ❖ **TAF/FTC/EVG/c** | 6 (6) | 0 | 6 (12) |
| Historical GT vs Proviral DNA NGS | | | |
| M184V/I on Historical GT, n (%): | 50 (50) | 50 (100) | 0 |
| Proviral DNA by NGS, n (%): | 70 (70) | 41 (82) | 29 (58) |
| • M184V/I present | 15 (21) | 15 (37) | 0 |
| • M184V/I absent | 55 (79) | 26 (63) | 29 (100) |
| • K65R present | 1 (1) | 1 (2) | 0 |
| • K65R present with Q151M | 1 (1) | 0 | 1 |

NGS = Next-Generation Sequence; Performed by Quest Diagnostics; Resistance-associated mutations present in 10% or more of viral species sequenced are reported.

Blick et al. AIDS 2024; Munich, Germany. Oral presentation OAX0903LB.

# Virologic Outcomes: Secondary Endpoints, 48 & 96W, and Week 144, ITT-E

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# Adherence to and Forgiveness of 3TC/DTG in a Real-World Cohort

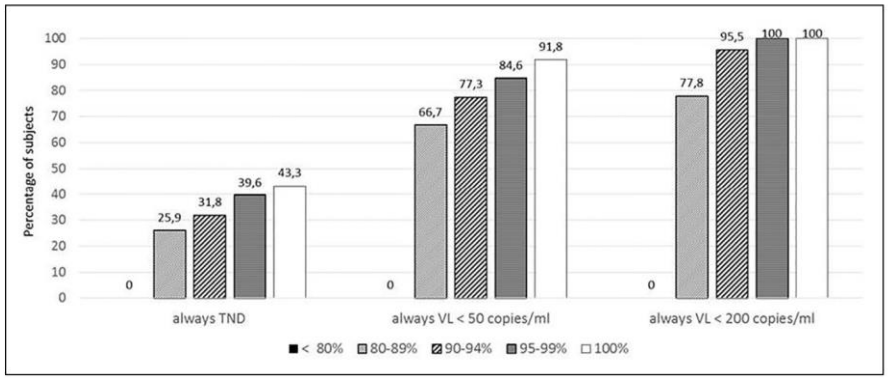
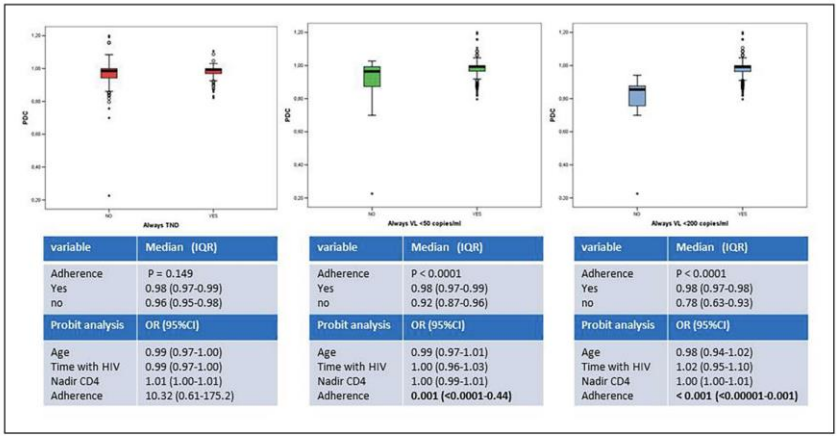



**Figure 1.** Virologic response expressed as achievement and constant maintenance of different HIV-RNA thresholds according to the individual adherence level as calculated by means of PDC.




| variable | Median (IQR) |
|---|---|
| Adherence | P = 0.149 |
| Yes | 0.98 (0.97-0.99) |
| no | 0.96 (0.95-0.98) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 0.99 (0.97-1.00) |
| Time with HIV | 0.99 (0.97-1.00) |
| Nadir CD4 | 1.01 (1.00-1.01) |
| Adherence | 10.32 (0.61-175.2) |

| variable | Median (IQR) |
|---|---|
| Adherence | P < 0.0001 |
| Yes | 0.98 (0.97-0.99) |
| no | 0.92 (0.87-0.96) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 0.99 (0.97-1.01) |
| Time with HIV | 1.00 (0.96-1.03) |
| Nadir CD4 | 1.00 (0.99-1.01) |
| Adherence | **0.001 (<0.0001-0.44)** |

| variable | Median (IQR) |
|---|---|
| Adherence | P < 0.0001 |
| Yes | 0.98 (0.97-0.98) |
| no | 0.78 (0.63-0.93) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 0.98 (0.94-1.02) |
| Time with HIV | 1.02 (0.95-1.10) |
| Nadir CD4 | 1.00 (1.00-1.01) |
| Adherence | **< 0.001 (<0.00001-0.001)** |

**Figure 2.** Box plot representation of PDC in PLWH achieving and maintaining a given virologic threshold compared to those that do not. Median adherence values and factors significantly associated with the outcome of interest according to probit analysis.

Maggiolo et al. Journal of the International Association of Providers of AIDS Care. 2022

# PASO-DOBLE (GeSIDA 11720)

Phase IV, open-label, multicentre, randomised clinical trial[1]

**30 sites across Spain**

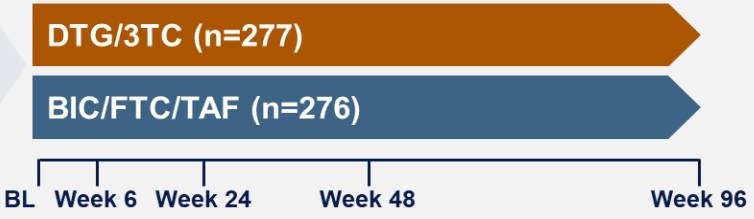
Collaborative study between **Fundación SEIMC-GeSIDA** and ViiV Healthcare

**Screening**

- HIV-1 RNA <50 c/mL for ≥24 weeks
- Current ART containing >1 pill/day, cobi booster, EFV or TDF
- No prior VF or known/suspected resistance
- No prior DTG or BIC
- No chronic hepatitis B

**Randomised 1:1**

Stratified by BL TAF use and sex at birth




**Primary endpoint:** Participants with plasma HIV-1 RNA ≥50 c/mL (FDA Snapshot; non-inferiority margin 4%)
**Key secondary endpoint:** Weight change (study was powered to assess differences)

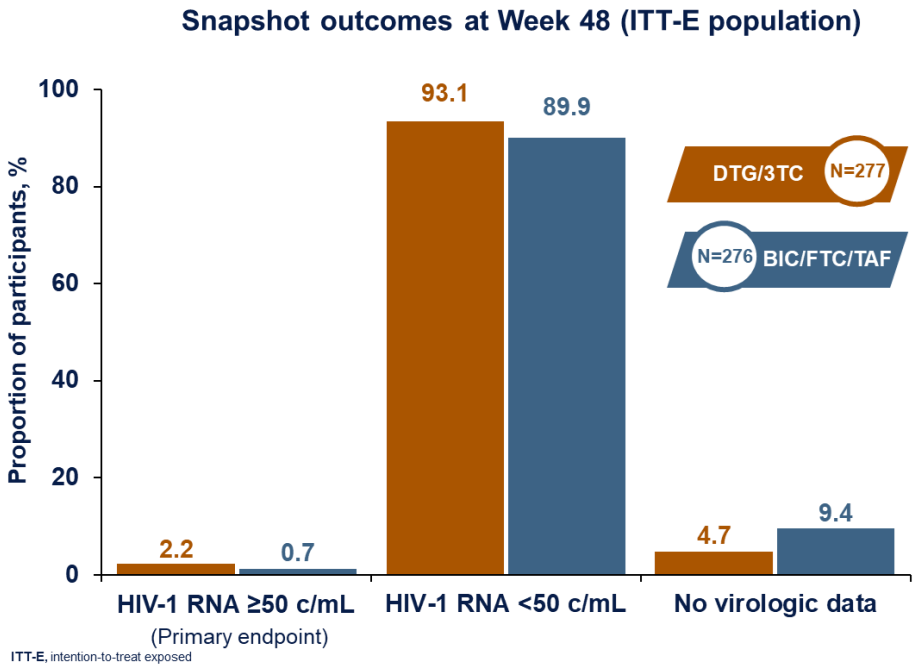
**Other secondary endpoints include efficacy, safety, tolerability, immune recovery, metabolic parameters, kidney function, blood pressure, body composition and bone mineral density, PROs, and genotypic resistance analysis in case of virological failure**

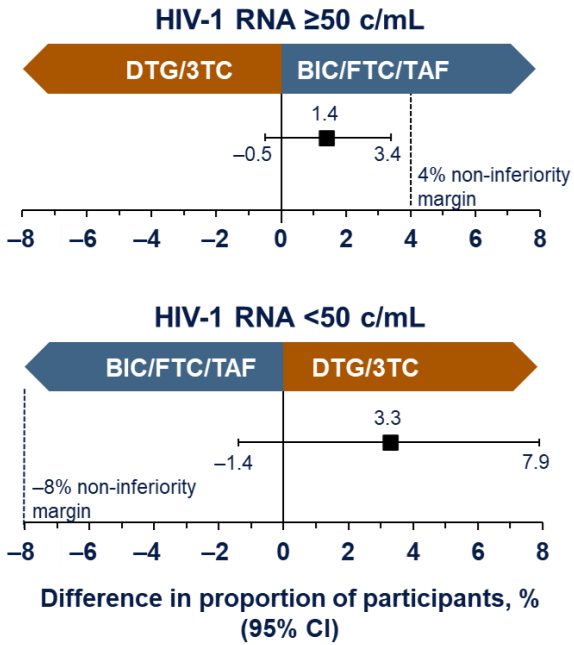
**Four sub-studies:** Omics | Senescence | Fat biopsies | Liver steatosis

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04884139. Accessed July 26, 2024.

Ryan et al. AIDS 2024; Munich, Germany. Oral presentation OAB3606LB.

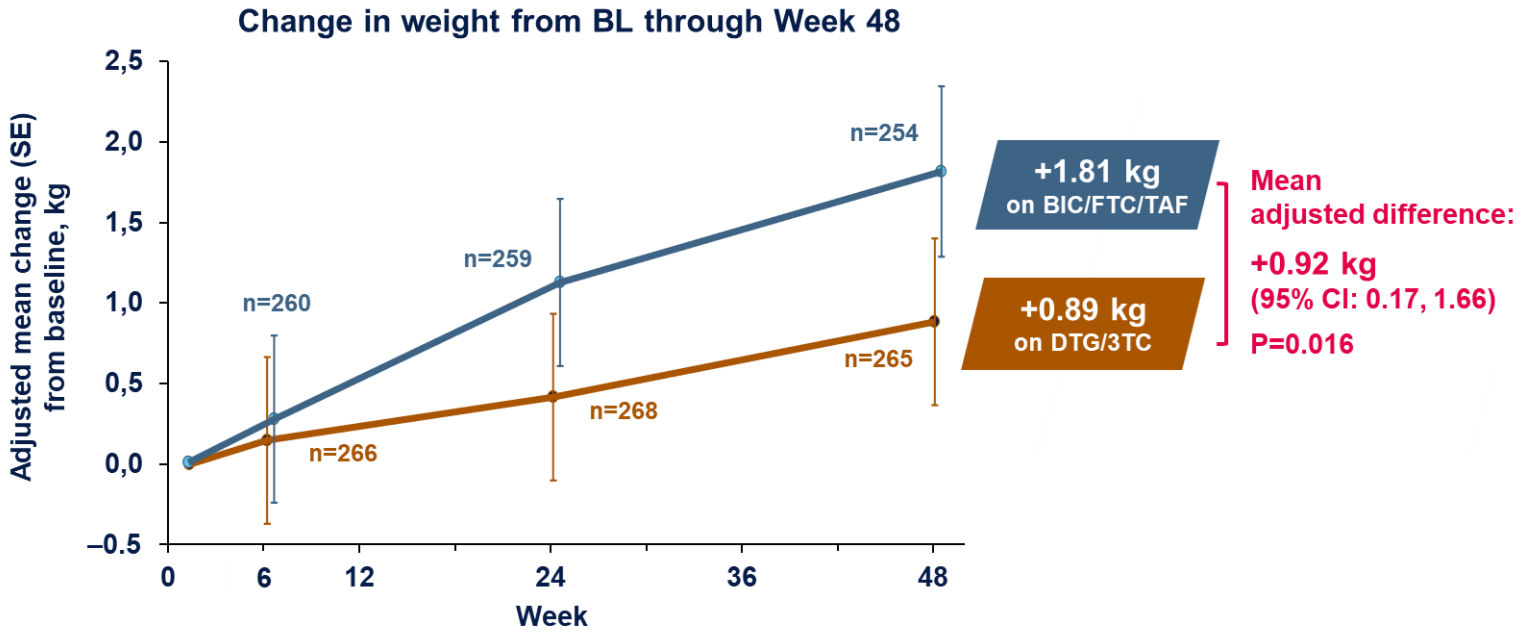
# PASO-DOBLE Study: Virologic Efficacy




Ryan et al. AIDS 2024; Munich, Germany. Oral presentation OAB3606LB.

# PASO-DOBLE Study: Weight Change

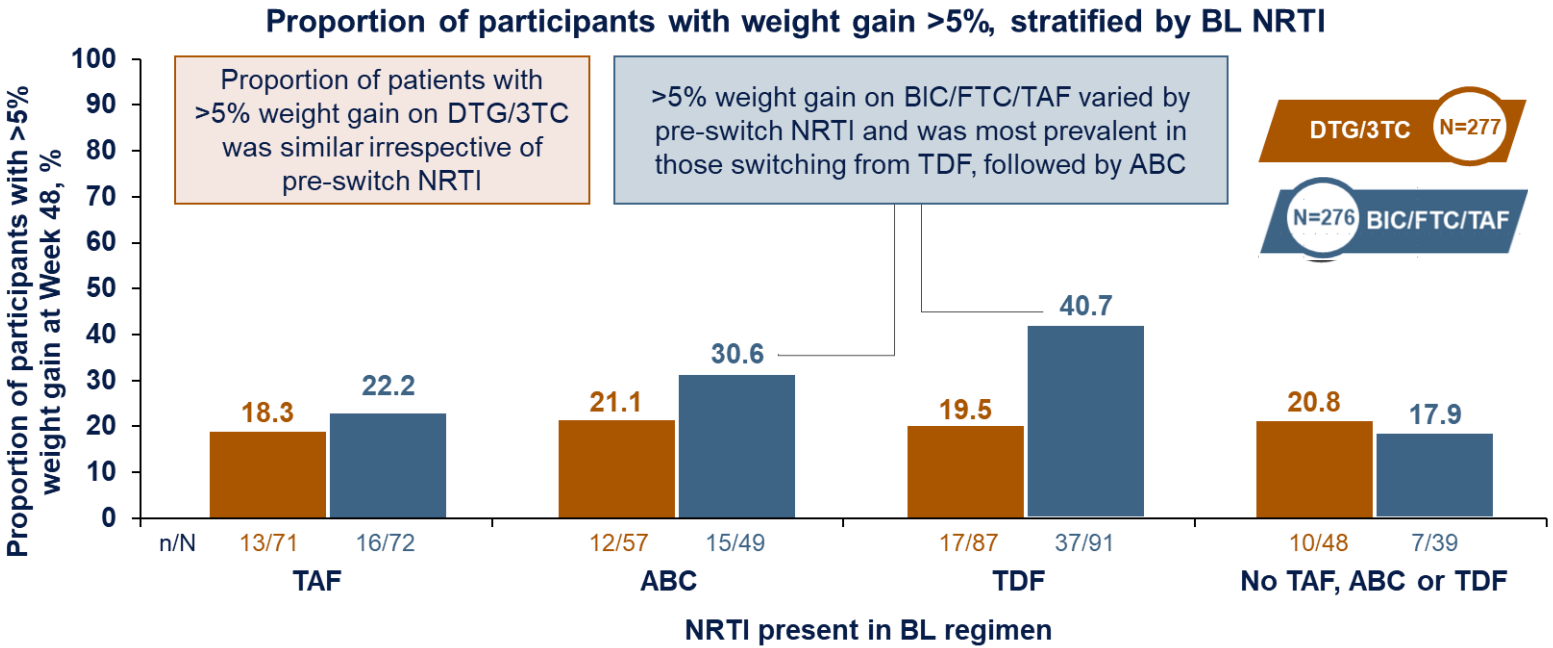



Adjusted by baseline value, sex, presence of TAF in previous ART, age and ethnicity.

The only association that was statistically significant in the model was treatment group.

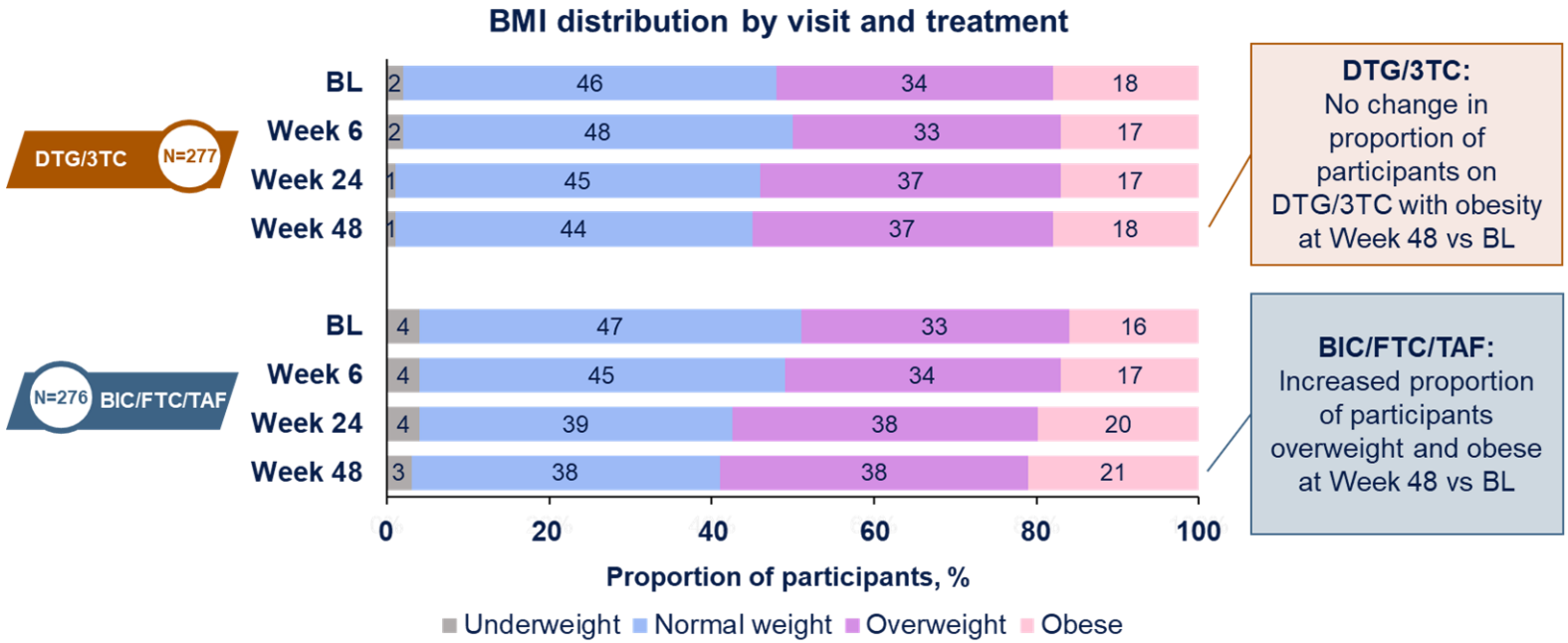
Ryan et al. AIDS 2024; Munich, Germany. Oral presentation OAB3606LB.

# PASO-DOBLE Study:
# Weight Gain >5% by Pre-switch NRTI 1




Ryan et al. AIDS 2024; Munich, Germany. Oral presentation OAB3606LB.

# PASO-DOBLE Study: BMI Distribution by Visit




Ryan et al. AIDS 2024; Munich, Germany. Oral presentation OAB3606LB.

Coorte Policlinico Gemelli

Real Life

# EFFECTIVENESS OF BIC/FTC/TAF AS SWITCH STRATEGY IN VIROLOGICALLY SUPPRESSED: REAL WORLD DATA FROM MONOCENTRIC COHORT

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Retrospective monocentric cohort study (Policlinico Gemelli), 431 pz

**Inclusion criteria**
**- switching to TAF/FTC/BIC after reaching virological suppression (HIV-RNA < 50 cp/mL)**
**- period 2018-2022 (36 months of follow-up time after switch)**

**Exclusion criteria**
**- patients with no follow-up visits**

**N = 431**

**ART-experienced PLWH who switched for the first time to B/F/TAF**

**Outcomes**

**Primary endpoint**: TF (VF and TD for any reason). **Secondary endpoints** included time to VF and TD; change in CD4, CD4/CD8; residual virema, metabolic and renal profile

Jan 2018–
Dec 2022

**PRIMARY ENDPOINTS**: Treatment failure as
1) virological failure (VF, i.e. 2 consecutive HIV-RNA ≥ 50 cp/mL or a single HIV-RNA ≥ 200 cp/mL)
2) treatment discontinuation (TD) for any reason

**SECONDARY ENDPOINTS:** Viro-immunological effectivness: 1) **Time to VF** and key **predictors** for VF; 2) **Changes** in **CD4** and **CD4/CD8** up to 36 (±3) months from switch and **predictors** of poor immunologic recovery; 3) For those who remain **virosuppressed**: **HIV RNA undetectable** or **residual viremia** up to 36 (±3) months from switch *(under analysis)*; tolerability and safety: 4) **TD for toxicity/intolerance** and **time to TD**; 5) **metabolic profile**: delta of total cholesterol and delta of TC/HDL up to 36 (±3) months from switch *(under analysis)*; 6) **renal profile**: **delta of creatinine** up to 36 (±3) months from switch *(under analysis)*

# Patient's characteristics at baseline

| Variables | BIC group (n=431) |
|---|---|
| Age, median (IQR) | 55 (46-61) |
| Male sex, n (%) | 295 (68.45) |
| HIV risk factors: Hetero | 191 (44.32) |
| CDC stage C, n (%) | 148 (34.34) |
| Median Time since HIV diagnosis (years), (IQR) | 18.2 (8.2-26.6) |
| Median Time of viral suppression (y), (IQR) | 6.0 (2.7-12.1) |
| Median CD4+ cell at baseline (IQR) | 615 (450-820) |
| Median CD4/CD8 ratio | 0.25 (0.09-0.40) |
| HCV coinfected | 66 (15.31) |
| HBV coinfected | 16 (3.71) |
| HIV viral subtype B, n (%) | 176 (40.84) |
| Median Time of cumulative exp to ARVs (y), (IQR) | 14.0 (7.0-23.0) |
| At least one previous failure, n (%) | 224 (51.97) |
| Previous failure with a INI-based regimen, n (%) | 18 (4.17) |
| Nadir CD4 (cell/µL) <200, n (%) | 239 (55.45) |
| Zenith HIV-RNA (cp/mL)>500000cp, n (%) | 47 (10.90) |

*ARV: 2NRTI+INI (294, 68%); Reason stop previous ARV: Pro-active switch (356, 83%)*

# RESULTS (VF)

**16 VF occurred during 22 months of median follow-up time (2.0 per 100 patients-years follow-up)**

**Figure 1.** Estimated probability of VF

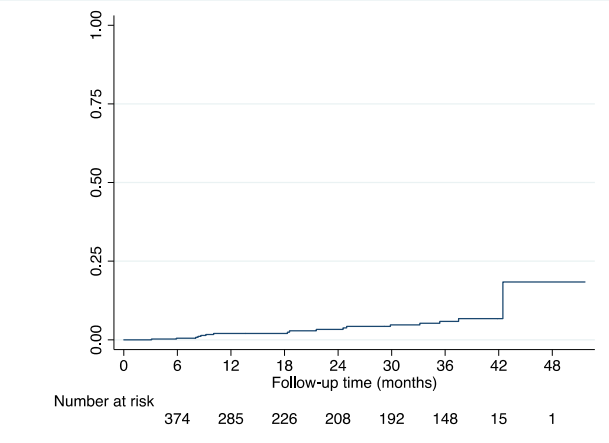



**Table 1.** Probabilities of VF at 1, 2 and 3 years

| Follow-up time | Estimated probabilities of VF |
|---|---|
| **1 Year** | 2.0% (95% CI 1.0%-4.2%) |
| **2 Years** | 2.9% (95% CI 1.5%-5.6%) |
| **3 Years** | 5.5% (95% CI 3.2%-9.2%) |

**Caucasian ethnicity** (versus others, aHR 0.32, 95% CI 0.11-0.94; p= 0.039) and a history of **previous VF** (versus none, aHR 10.06, 95% CI 1.32-76.56; p = 0.026) independently **predicted VF.**

# Details of virological failures

| Age | Sex | Therapy pre-switch | VF viremia (cp/mL) | Good adherence reported | Time to virological suppression (months) |
|---|---|---|---|---|---|
| **43** | M | FTC/TAF/EVG/c | 213 | no | 6 |
| **52** | F | FTC/TAF+RAL | 1.634 | yes | Treatment discontinued |
| **59** | M | FTC/TAF/RPV | 10.000.001 | no | 10 |
| **53** | F | FTC/TAF/EVG/c | 18.359 | no | 1 |
| **45** | M | FTC/TAF/EVG/c | 210 | no | 18 |
| **53** | M | FTC/TAF+DTG | 58; 225.891 | no | Treatment discontinued |
| **76** | F | 3TC/ABC/DTG | 778 | yes | 1 |
| **62** | M | FTC/TAF+RAL | 63; 116 | no | 18 |
| **45** | F | DRV/c + TDF | 505 | no | Treatment discontinued |
| **35** | M | FTC/TAF+RAL | 424.283 | no | 5 |
| **54** | M | FTC/TAF/EVG/c | 15.676 | yes | Treatment discontinued |
| **44** | F | FTC/TAF/EVG/c | 21.718 | no | 1 |
| **50** | F | ABC/3TC+ATZ/r | 109; 98 | no | 15 |
| **54** | F | FTC/TAF+DTG | 1.340.468 | no | Treatment discontinued |
| **35** | M | FTC/TAF/EVG/c | 1.639 | unknown | 18 |
| **55** | M | FTC/TAF+DTG | 1.407 | yes | 6 |

# RESULTS (TD)

- Discontinuation occurred in 42 cases (5.0 per 100 patients-year of follow-up)

**Figure 2.** Estimated probability of TD

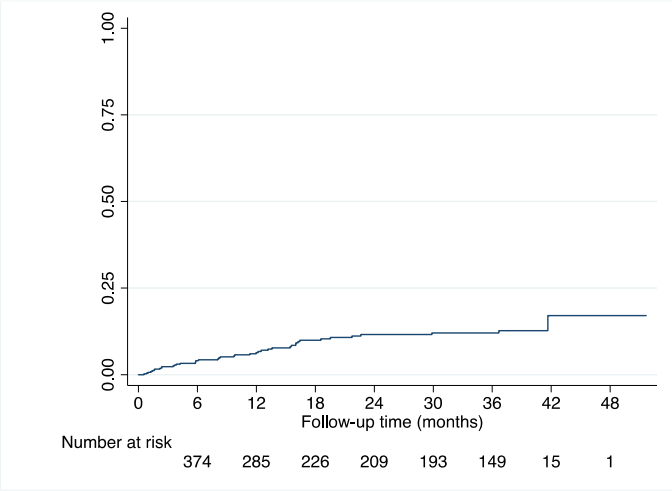
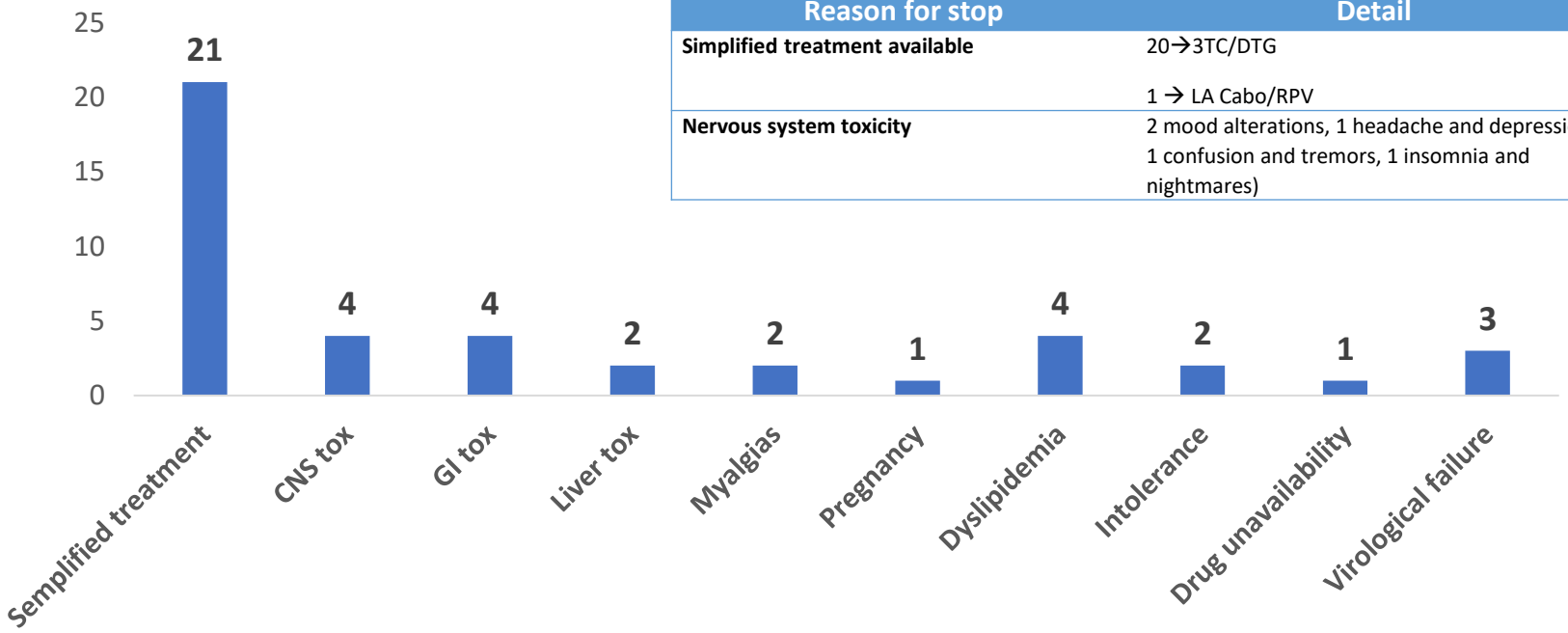



**Table 2**. Probability of TD at 1, 2 and 3 years.

| Follow-up time | Estimated probabilities of VF |
|---|---|
| 1 Year | 2.0% (95% CI 1.0%-4.2%) |
| 2 Years | 2.9% (95% CI 1.5%-5.6%) |
| 3 Years | 5.5% (95% CI 3.2%-9.2%) |

No predictors of BIC/FTC/TAF discontinuation were identified.

# Details of treatment discontinuation




| Reason for stop | Detail |
|---|---|
| **Simplified treatment available** | 20→3TC/DTG<br><br>1 → LA Cabo/RPV |
| **Nervous system toxicity** | 2 mood alterations, 1 headache and depression, 1 confusion and tremors, 1 insomnia and nightmares) |

# RESULTS (CD4)

An **increasing trend in CD4** count over 3 years was evidenced (p=0.095) (fig.3)

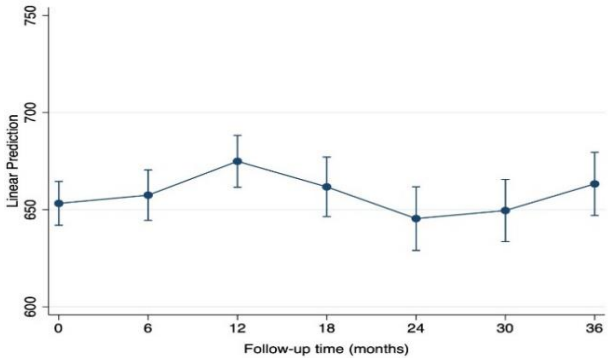



Fig. 3: trend CD4 count from MO to M36

**Nadir CD4 count < 200** cell/µL (compared with nadir >200, B: -55, 95%CI -96 - -13; p=0.011)
**Injection drug users** as a risk factor of HIV infection (versus others, B: -47, 95% CI -87 - -8; p=0.019)
**Higher CD4 count** at switch (per 100 cells/mL more, B: -15, 95% CI -22 - -9; p<0.001)

were associated with a **reduction in delta CD4 count at 12 months**

# RESULTS (CD4/CD8)

An increase in CD4-to-CD8 ratio over 3 years was evidenced (p<0.001). (fig.4)

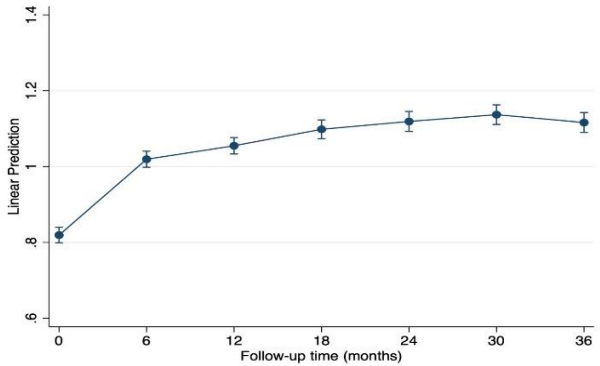



Fig. 4: trend CD4/CD8 from M0 to M36.

A **history of AIDS** (versus none, B: -0.10, 95% CI -0.18 - -0.01; p=0.037) and

**longer time of virological suppression** (per 1 year more, B: -0.02, 95% CI - 0.02 - -0.01; p<0.001)

were associated with a **reduction in delta CD4-to-CD8** at 12 months.

# CONCLUSIONS

1) **BIC/FTC/TAF** as switch strategy demonstrated **high effectiveness**, **tolerability** and **safety** in real-life with **4.4% VF, 2.2% VF at 1-year, 3.5% TD for toxicity**.

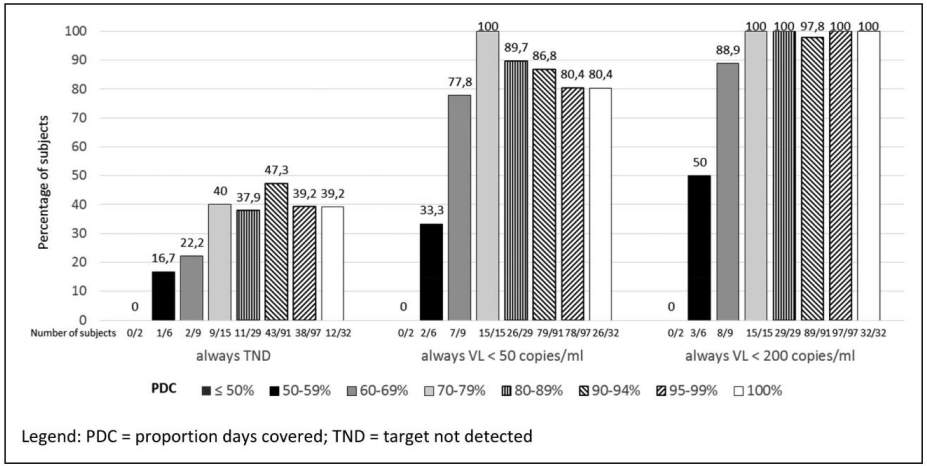
2) Main cause of discontinuation was simplification. **No discontinuation due to VF** was reported.

1) These data should be confirmed with long-term follow-up

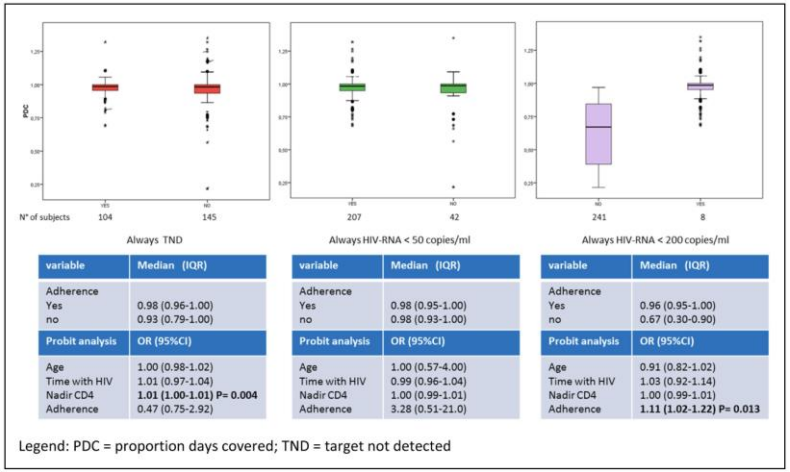
# Real World Data on Forgiveness to Uncomplete Adherence to Bictegravir/ Emtricitabine/Tenofovir Alafenamide

- Retrospective, monocentric study of PLWH ever treated with B/F/TAF from January 2020 to March 2022.
- Patients with a minimum of 2 drugs refills were included irrespective of the length of their follow-up.
- Adherence was measured by means of percent day covered (PDC).
  - PDC is the number of days with medication available divided by the number of days in a specified time interval.
  - The denominator of PDC is typically a clinically meaningful number of days that in our case was the whole follow-up period. To calculate PDC a minimum of 2 refills are needed and PDC may be summarized as a continuous outcome or categorical

# Results




Legend: PDC = proportion days covered; TND = target not detected




| variable | Median (IQR) |
|---|---|
| Adherence | |
| Yes | 0.98 (0.96-1.00) |
| no | 0.93 (0.79-1.00) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 1.00 (0.98-1.02) |
| Time with HIV | 1.01 (0.97-1.04) |
| Nadir CD4 | **1.01 (1.00-1.01) P= 0.004** |
| Adherence | 0.47 (0.75-2.92) |

| variable | Median (IQR) |
|---|---|
| Adherence | |
| Yes | 0.98 (0.95-1.00) |
| no | 0.98 (0.93-1.00) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 1.00 (0.57-4.00) |
| Time with HIV | 0.99 (0.96-1.04) |
| Nadir CD4 | 1.00 (0.99-1.01) |
| Adherence | 3.28 (0.51-21.0) |

| variable | Median (IQR) |
|---|---|
| Adherence | |
| Yes | 0.96 (0.95-1.00) |
| no | 0.67 (0.30-0.90) |
| **Probit analysis** | **OR (95%CI)** |
| Age | 0.91 (0.82-1.02) |
| Time with HIV | 1.03 (0.92-1.14) |
| Nadir CD4 | 1.00 (0.99-1.01) |
| Adherence | **1.11 (1.02-1.22) P= 0.013** |

Legend: PDC = proportion days covered; TND = target not detected

B/F/TAF was very robust in forgiving lower adherence rates. Further, PDC, with the dispensing correction we adopted, could potentially overestimate adherence rates, as drug possession is not necessarily synonymous of effectively taking the drug.

Maggiolo et al. Journal of the International Association of Providers of AIDS Care, 2022

# COMPARING EFFICACY, SAFETY AND TOLERABILITY OF 3TC/DTG, TAF/3TC/DOR AND TAF/FTC/BIC IN SWITCH STRATEGY OF VIROLOGICALLY SUPPRESSED HIV-INFECTED PEOPLE.

Farinacci D et al. Poster Presentation ICAR 2023
Farinacci D et al. Submitted AIDS R

We collected and analyzed data from HIV-infected patients followed at a single center in Rome, **permanently suppresed (with HIV-RNA < 50 copies/mL for at least 6 months) who switched therapy to:**

3TC/DTG

TAF/3TC/DOR

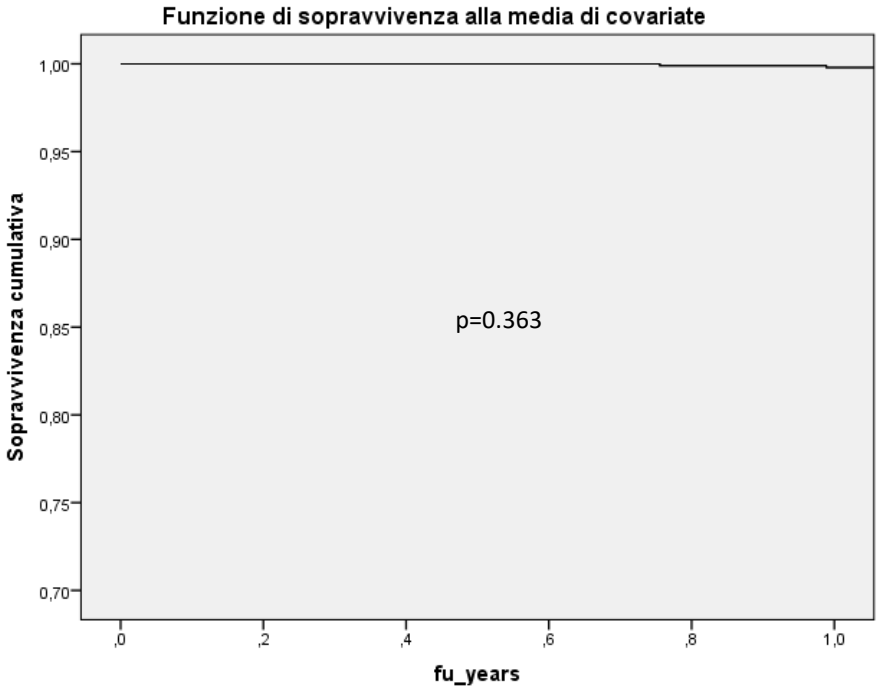
TAF/FTC/BIC

| Variables | DTG group (n=1006) | BIC group (n=319) | DOR group (n=47) | p |
|---|---|---|---|---|
| **Male sex, n (%)** | 707 (70.3) | 226 (70.8) | 30 (63.8) | 0.611 |
| **Years of age, median (IQR)** | 52.6 (43.7-58.7) | 53.9 (45.8-58.8) | 50.6 (42.8-56.5) | 0.185 |
| **HIV risk factor, n (%):** | | | | |
| - **MSM** | 416 (41.4) | 116 (36.4) | 16 (34.0) | |
| - **Heterosexual** | 414 (41.2) | 132 (41.4) | 24 (51.1) | 0.095 |
| - **IDUs** | 92 (9.1) | 47 (14.7) | 4 (8.5) | |
| **Years of HIV, median (IQR)** | 14.6 (7.7-22.2) | 16.2 (6.0-24.1) | 12.3 (5.1-21.6) | 0.194 |
| **Years of ARV exposure, median (IQR)** | 11.8 (6.4-19.5) | 11.9 (5.1-21.0) | 10.9 (3.8-18.1) | 0.327 |
| **CDC stage C, n (%)** | 271 (26.9) | 127 (39.8) | 14 (29.8) | **<0.001** |
| **Ab anti-HCV, n (%)** | 119 (11.8) | 51 (16.0) | 3 (6.4) | 0.069 |
| **Years of virological suppression, median (IQR)** | 8.7 (4.3-13.3) | 6.1 (2.7-12.0) | 5.7 (2.5-13.4) | **<0.001** |
| **Zenith HIV-RNA (log10), median (IQR)** | 4.83 (4.17-5.36) | 4.99 (4.25-5.41) | 5.32 (4.57-5.70) | **0.007** |
| **CD4+ cell nadir, median (IQR)** | 220 (89-328) | 164 (46-310) | 161 (41-264) | **<0.001** |
| **Previous VF, n (%)** | 386 (38.4) | 149 (46.7) | 12 (25.5) | **0.004** |
| **Baseline CD4+ cell count, median (IQR)** | 681 (524-857) | 614 (426-833) | 717 (478-825) | **0.004** |
| **Previous ARV regimen, n (%):** | | | | **<0.001** |
| - **2NRTI+INI** | 298 (29.6) | 245 (76.8) | 20 (42.6) | |
| - **2NRTI+NNRTI** | 150 (14.9) | 38 (11.9) | 19 (40.4) | |
| - **2NRTI+PI** | 34 (3.4) | 11 (3.4) | 6 (12.8) | |
| - **3TC-based 2DR** | 479 (47.6) | 19 (5.9) | 2 (4.2) | |
| - **Other** | 45 (4.5) | 6 (1.9) | / | |

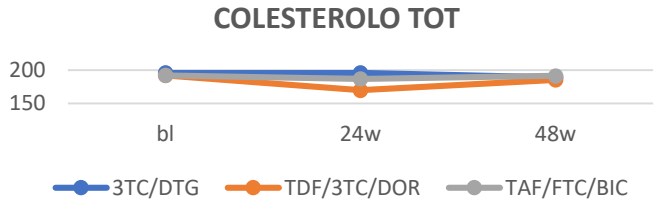
# Virological failures

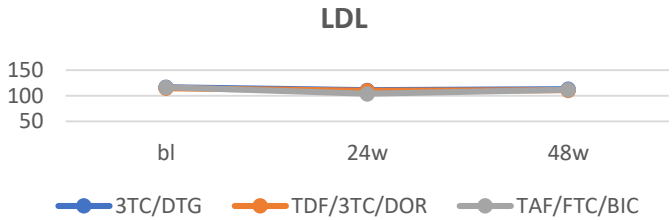
- 9 cases of VF (2 HIV-RNA > 50 copies/mL or 1 HIV-RNA > 1000 copies/mL)

- All three groups maintain virological suppression in 99% of cases after 48 weeks, with no differences between regimens (p=0.363)



# Metabolic profile

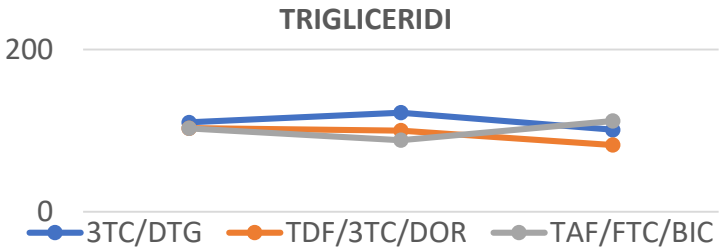



In two groups we as reduction in total cholesterol:

- - 4,5 mg/dL in DTG ($p<0.001$)
- - 17,2 mg/dL in DOR ($p=0.013$)
- -In BIC group reduction was NS

Regarding LDL we found: -3 mg/dL in DTG ($p=0.017$)




DOR causes the most important decrease in triglyceridies (- 20,6 mg/dL, $p=0.027$)

# CONCLUSIONS

- Nell'ambito della semplificazione le strategie indicate dalle lineeguida mostrano efficacia e tollerabilità nel lungo termine

- Gli studi ancora non riescono a dirci QUANDO è il tempo di semplificare e mancano i dati sulla semplificazione PRECOCE

- Siamo in un' epoca per l'infezione da HIV dove è necessario un cambiamento nel nostro modo di pensare e approcciarci……..è arrivato il momento di superare il binomio HIV-RNA e CD4 come parametri di monitoraggio e andare a valutare il processo infiammatorio? HIV-DNA, citochine proinfiammatorie, ampliamento degli algoritmi per il rischio CV, multidisciplinarietà?

- Le strategie LA cambieranno il modo di effettuare la semplificazione o renderanno ancor più complesso gestire una terapia ARV che deve essere sempre più personalizzata?

Grazie per l’attenzione