L’ ART nel 2022

Simona Di Giambenedetto
Università Cattolica del Sacro Cuore di Roma
Fondazione Gemelli, IRCCS, Roma

Disclosures

- I have received funding for Advisory Board, Spekear Panels and for preparation of educational materials from the following:

- Gilead Sciences
- ViiV Healthcare
- Jansenn-Cilag
- Merck Sharp & Dohme

Strategie per successo della terapia ARV

- Iniziare bene…e presto
- Farmaci con alta efficacia e tollerabilità
- TERAPIA PERSONALIZZATA

Cosa si intende per Rapid-ART

- Con il termine di Rapid-ART si intende un intervento sanitario che porti ad un inizio rapido della terapia antivirale in soggetti sieropositivi, idealmente prima dei risultati degli esami ematochimici classici (genotipo HIV, HLA, viremia e conta CD4+).

- Benchè il termine di per sé non ponga limiti cronologici, esempio più lampante della strategia in questione è rappresentato dal Test&Treat, l'inizio della terapia il giorno stesso della conferma della positività al test sierologico per HIV.

Rapid Start – Potential Benefits and Limitations

Potential Benefits

- Better clinical outcomes due to less time off ART
- Engagement opportunity to increase retention in care
- Shorter time to treatment decreases anxiety, increases trust
- Public health benefit: decreased transmission risk

Potential Limitations

- ART may not be optimized (renal insufficiency)
- OIs requiring delayed ART may not be ruled out
- Less time to address barriers to ART and adherence
- Risk of resistance if low barrier regimen used
- Requires change in work-flow with rapid access (access, appointment scheduling, staffing)

Further implementation research will continue to provide a better understanding of benefits and limitations in real world settings

- DHHS, IAS-USA, EACS

Recommendations for Rapid/Immediate ART Initiation

IAS-USA 2020[1]	DHHS 2019[2, 3]	EACS 2020[4]
• ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART* or for those with unclear HIV diagnosis • Only triple therapy is recommended for rapid ART start	• ART should be started immediately or as soon as possible after diagnosis for adults and children of all ages • Only triple therapy is recommended for rapid ART start	• ART is recommended in all adult PLWH irrespective of CD4 counts • If ART is to be initiated before genotypic testing results are available, it is recommended to select a first line regimen with a high barrier to resistance
Recommended Regimens		
BIC/FTC/TAF	**BIC/FTC/TAF**	**BIC/FTC/TAF**
DTG + TAF/FTC or TDF/(FTC or 3TC)	DTG + TAF/FTC or TDF/(FTC or 3TC)	DTG + TAF/FTC or TDF/(FTC or 3TC) or ABC/3TC†
	DRV/b + TAF/FTC or TDF/(FTC or 3TC)	PI/b + TAF/FTC or TDF/(FTC or 3TC) or ABC/3TC†

* Unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated
DHHS: NNRTIs should not be used because of concerns about transmitted drug resistance. Transmitted mutations conferring NNRTI–R are more likely than those associated with PI or INSTI-R
DHHS: Preferred regimens for children ≤ 12 years in addition to those above include: two NRTIs plus RAL or EVG/c or LPV/r, ATV/r, or NVP depending on age and weight
† For primary HIV infection, a combination of TDF or TAF, FTC, and either DRV/b, DTG or BIC should be considered for treatment initiation prior to genotype testing results. PI/b + TAF/FTC or TDF/FTC or ABC/3TC and regimens with TDF/3TC and ABC/3TC are only recommended by EACS for rapid initiation in PLWH with chronic infection. ABC contraindicated if HLA-B*57:01 positive. Even if HLA-B*57:01 negative, counselling on HSR risk still mandatory. ABC should be used with caution in persons with a high CVD risk (> 10%).

1. Saag MS, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults: 2020 Recommendations of the International Antiviral Society–USA Panel. JAMA. Published online October 14, 2020. https://jamanetwork.com/journals/jama/fullarticle/2771873
2. DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, December 2019. Accessed October 2020
3. DHHS. Guidelines for the use of Antiretroviral Agents in Pediatric HIV Infection, April 2020. Accessed October 2020.
4. EACS. Guidelines Version 10.1, October 2020. http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html

Treatment | DTG + 3TC

STAT: Phase 3b, open-label, single-arm study (USA, W48)

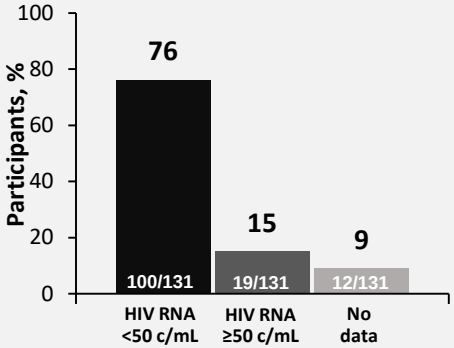
DTG/3TC for Rapid Start

ART-naïve adult PLWH (diagnosed ≤14 days of study entry) N=131 DTG/3TC

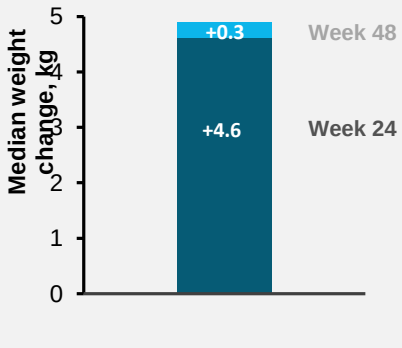
Key Secondary Outcomes at W48
Proportion of participants with plasma HIV-1 RNA <50 c/mL: FDA snapshot, ITT-E M=F, Observed analyses. Safety (AEs, DRAEs, discontinuations)

2019–2020

HIV-1 RNA <50 c/mL, W48 (FDA Snapshot)



Weight Increase, W48



Efficacy <50 c/mL, Observed Analysis: **97% (107/110)**
Efficacy <50 c/mL, ITT-E (M=F) Analysis: **82% (107/131)**

Grade 2–5 DRAEs (2%); serious AEs (2%)

10 (8%) PLWH switched from DTG/3TC by W48

- 5 HBV, 1 M184V, 1 AE (rash), 2 withdrew, 1 pregnancy
- 9/10 switched to 3-drug regimen
- +2 switches post-W48 (lack of efficacy; nonadherence)

18 (14%) participants discontinued the study

- 11% lost to follow-up or withdrew consent
- 3% investigator decision

No treatment-emergent resistance detected

The efficacy of DTG/3TC for rapid start was 76% (FDA Snapshot) after 48 weeks
Weight gain was +4.9 kg; treatment modifications due to baseline lab results (HBV, M184V) in 5%

- AE, adverse event; BL, baseline; DRAE, drug-related adverse event; ITT-E, intent to treat–exposed; M=F, missing=failure

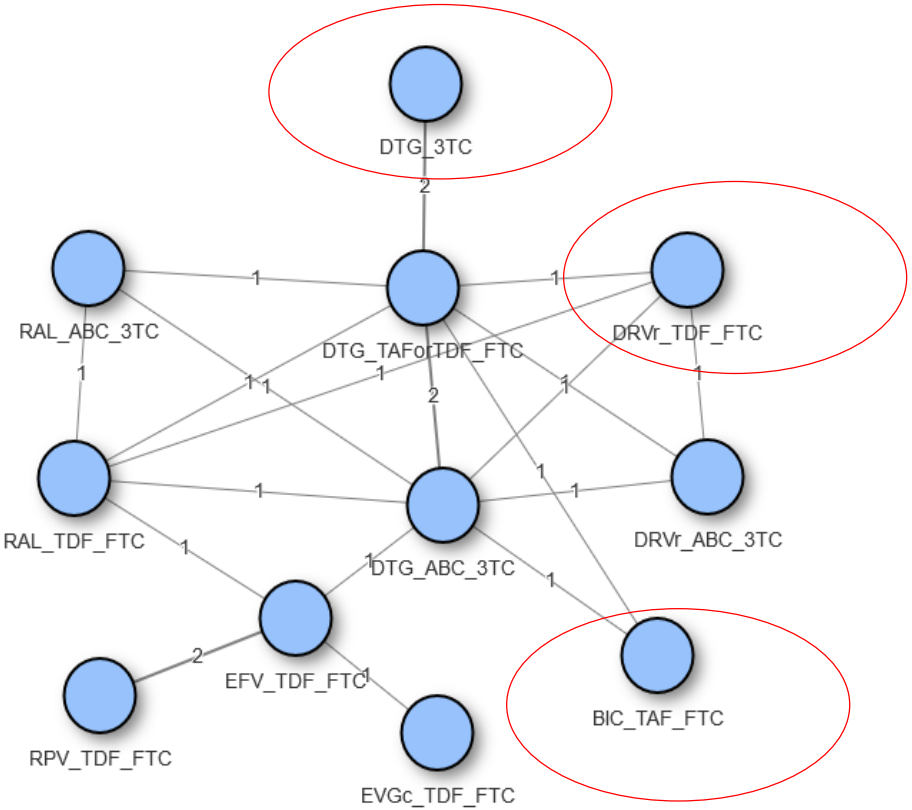
- Rolle CP, et al. IAS v2021, PEB182

Lineeguida EACS 2021

Regimen	Main requirements	Additional guidance (see footnotes)
Recommended regimens		
2 NRTIs + INSTI		
ABC/3TC + DTG ABC/3TC/DTG	HLA-B*57:01 negative HBsAg negative	I (ABC: HLA-B*57:01, cardiovascular risk) II (Weight increase (DTG))
TAF/FTC/BIC		II (Weight increase (BIC, TAF))
TAF/FTC or TDF/XTC + DTG		II (Weight increase (DTG, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing)
TAF/FTC or TDF/XTC + RAL qd or bid		II (Weight increase (RAL, TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) IV (RAL: dosing)
1 NRTI + INSTI		
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500,000 copies/mL Not recommended after PrEP failure	II (Weight increase (DTG)) V (3TC/DTG not after PrEP failure)
2 NRTIs + NNRTI		
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR		II (Weight increase (TAF)) III (TDF: prodrug types. Renal and bone toxicity. TAF dosing) VI (DOR: caveats, HIV-2)

Modificata da https://www.eacsociety.org/media/2021_guidelines-11.0_final.pdf

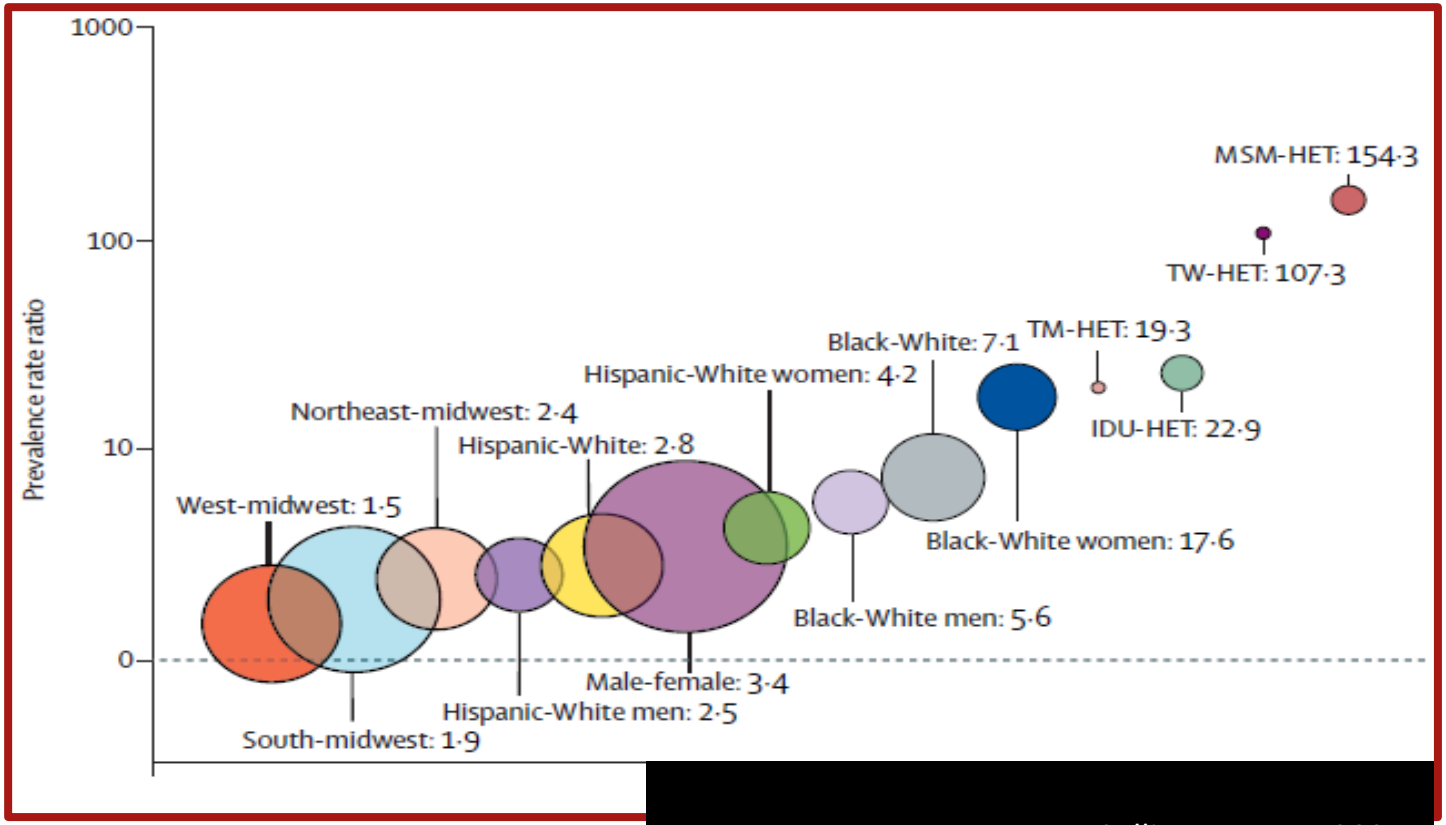
Network of Studies



TDF+3TC+DOR

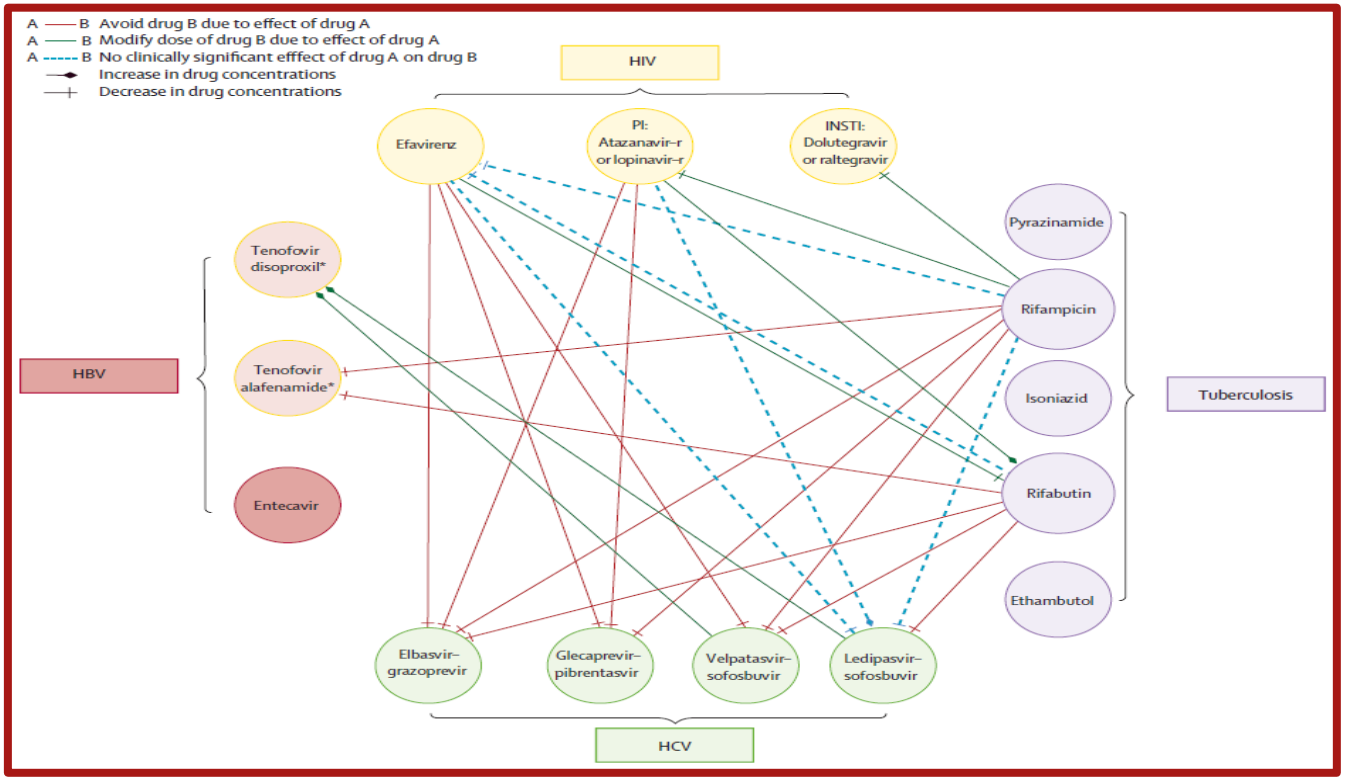
Nickel et al. AIDS 2020: Virtual. Poster PDB0104.

Magnitude of disparity in USA



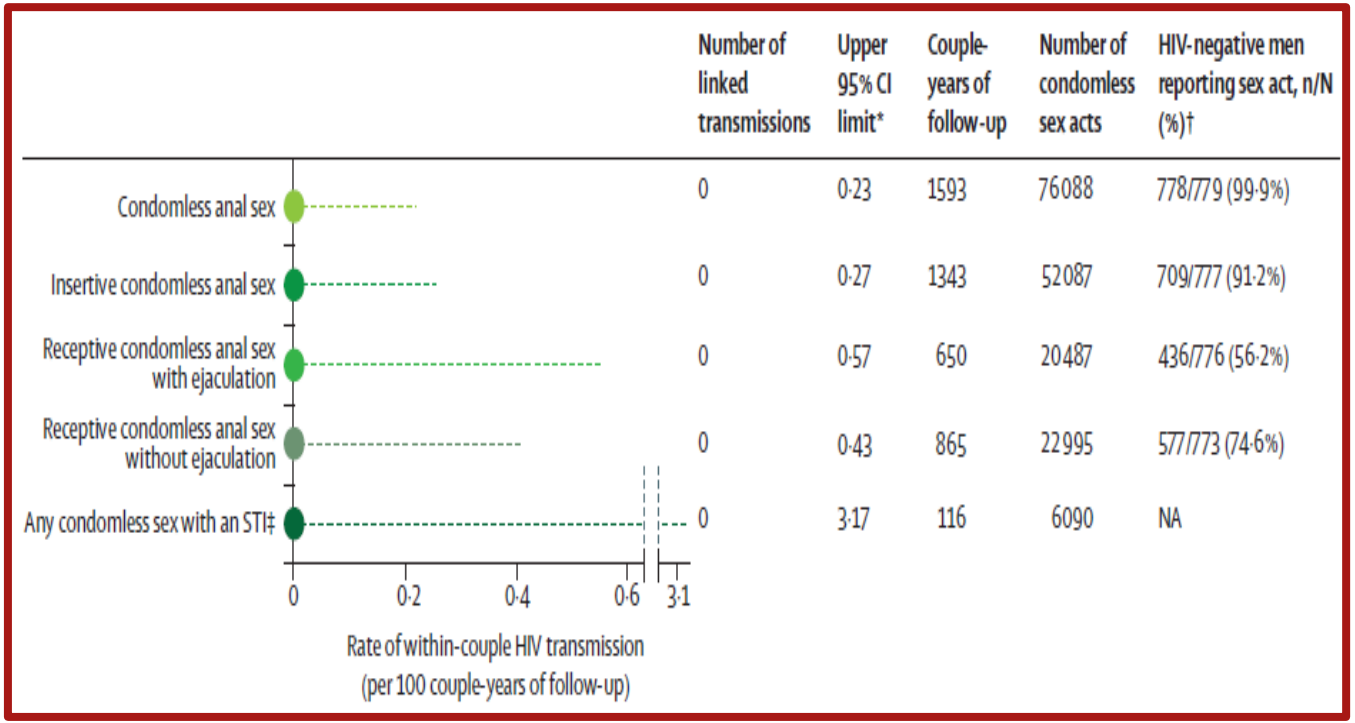
Sullivan, Lancet 2021

Complexities in the treatment of OI



U Arora, Lancet Infect Dis 2020

Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER)



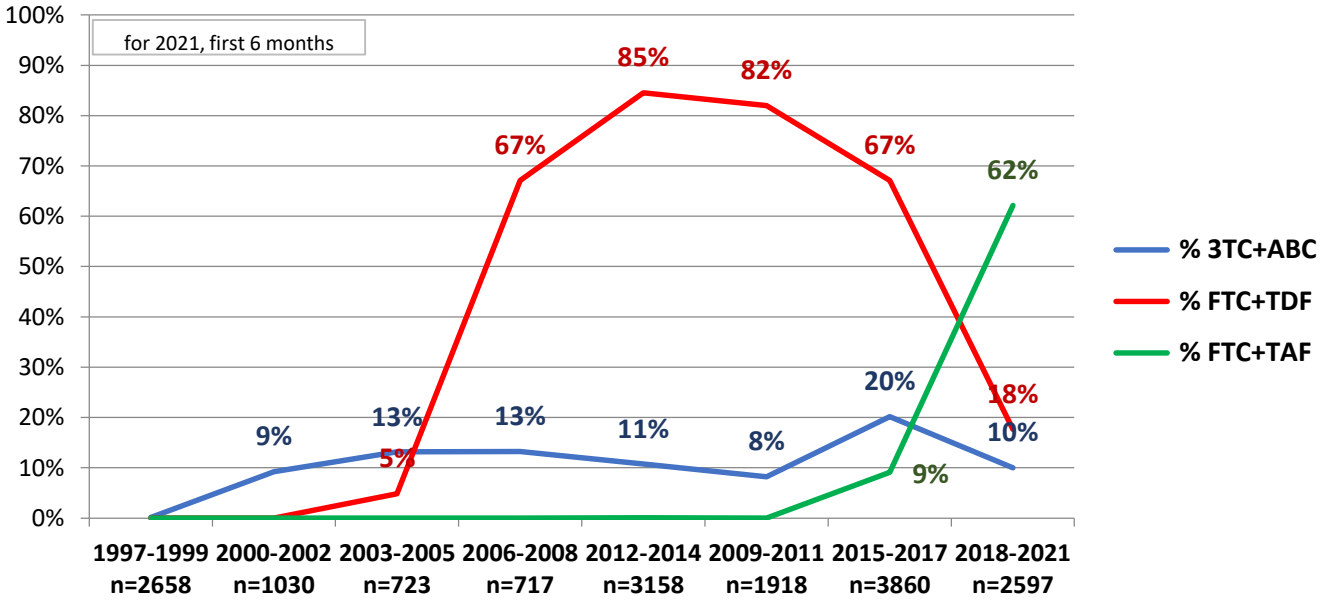
	Number of linked transmissions	Upper 95% CI limit*	Couple-years of follow-up	Number of condomless sex acts	HIV-negative men reporting sex act, n/N (%)†
Condomless anal sex	0	0·23	1593	76088	778/779 (99·9%)
Insertive condomless anal sex	0	0·27	1343	52087	709/777 (91·2%)
Receptive condomless anal sex with ejaculation	0	0·57	650	20487	436/776 (56·2%)
Receptive condomless anal sex without ejaculation	0	0·43	865	22995	577/773 (74·6%)
Any condomless sex with an STI‡	0	3·17	116	6090	NA

- **Three or more drugs 92%**
- **Dual therapy 5%**
- **Monotherapy 2%**

AJ Rodger, Lancet 2019

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Proportion of of patients treated with TDF/FTC or TAF/FTC or ABC/3TC as firstline backbone, according to calendar period



Jul 2021 Report

Pratica clinica

Comparing the efficacy and safety of dolutegravir+lamivudine vs bictegravir/emtricitabine/tenofovir alafenamide fumarate as first-line regimens in clinical practice

- Studio di pratica clinica su PLWHIV naive che hanno iniziato all’interno della coorte una terapia di prima linea con BIC/FTC/TAF o DTG/3TC

- Sono stati analizzati 44 pazienti, 22 per gruppo

Variables	Overall (n=44)	DTG group (n=22)	BIC group (n=22)	P
Males, n (%)	33 (75.0)	17 (77.3)	16 (72.7)	0.500
Years of age, median (IQR)	44 (31-56)	35 (25-53)	50 (36-57)	0.035
AIDS-defining event at diagnosis, n (%)	8 (18.2)	0	8 (36.4)	0.002
Anti-HCV antibodies, n (%)	0	0	0	/
HBV-coinfection, n (%)	0	0	0	/
Peak HIV-RNA, log10 copies/ml, median (IQR)	4.97 (4.61-5.33)	4.77 (4.38-4.99)	5.27 (4.97-5.86)	<0.001
Nadir CD4+ cell count, cell/mm3, median (IQR)	246 (89-417)	328 (243-460)	97 (43-268)	0.001
Baseline CD4/CD8 ratio, median (IQR)	0.34 (0.15-0.51)	0.45 (0.33-0.74)	0.21 (0.09-0.41)	0.009

Risultati-1

- Nel gruppo BIC e DT, la probabilità di rimanere virologicamente soppressi a 12 mesi è risultata essere del 91%.

- Non sono stati riscontrate sospensioni del regime.

- I due casi di FV nel gruppo BIC (mancata soppressione a 6 mesi) hanno mantenuto il regime e hanno ottenuto nei mesi successivi la soppressione dell'HIV-RNA.

Risultati-2

- Dal punto di vista immunologico, i pazienti hanno mostrato un incremento significativo della conta dei CD4+ sia a 6 mesi (+115 cell/mm3, p=0.001) che a 12 mesi (+218 cell/mm3, p=0.001). L'incremento a 12 mesi è risultato correlato ad un più alto zenith della carica virale (per 0.1 log10 copies/ml in più, +15.3 cell/mm3, 95%CI 1.8-28.8, p=0.030), ulteriormente confermando l'efficacia del regime nei pazienti con malattia avanzata.

- Hanno mostrato inoltre un incremento del rapport CD4/CD8 a 6 (+0.12, p=0.005) e 12 mesi (+0.20, p=0.001). L'incremento del rapport CD4/CD8 è risultato invece correlato al valore del rapport stesso alla diagnosi (per 0.10 in più, +0.20, 95%CI 0.04-0.27, p=0.013).

Conclusioni

- Anche nella pratica clinica della nostra coorte multicentrica, BIC/FTC/TAF e DT si sono dimostrati parimenti regimi efficaci e sicuri, con incrementi significativi dei parametri immunologici, in particolare in pazienti con malattia avanzata.

- Avere a disposizione regimi così efficaci e tollerabili in tutte le classi di pazienti naive al trattamento rappresenta un'arma fondamentale per i clinici, in particolare in periodi di difficile accesso al trattamento come durante la pandemia.

Principi della semplificazione

- **Principali finalità**
  - Ovviare a una tossicità in atto (switch reattivo)
  - Prevenire una tossicità prevedibile (switch preventivo o proattivo);
  - Favorire l'aderenza attraverso una riduzione in sicurezza del numero di compresse o di dosi;
  - Ovviare a interazioni farmacologiche sfavorevoli;
  - Eliminare necessità di assunzione di liquidi o cibi;
  - Permettere uso ottimale durante la gravidanza;
  - Ridurre i costi;
  - Protezione da infezione o riattivazione di HBV;
  - "Fortificazione" del regime

  - CAMBIARE PER TOGLIERE UN FARMACO DALLO SCHEMA?

- **Priorità**
  - **Mantenere la soppressione virologica;**
  - **Garantire che i benefici siano superiori ai potenziali rischi**

Attuali schemi di semplificazioni secondo linee guida

	EACS 10.0 (Nov 2019)	Linee guida SIMIT (2017)
DTG + RPV	**Supported by large trials**	**AI**
3TC + DTG	**Supported by large trials**	BII
Cabotegravir+RPV	**Supported by large trials**	_
3TC + bDRV	**Supported by large trials**	**AI→switch da PI** BI→ switch da altre classi
Alternativi		
DRVb + RPV	Supported by small trials	CI
DTG + bDRV	na	na

TDF+3TC+DOR

Modificata da https://www.eacsociety.org/media/2021_guidelines-1.0_final.pdf
Modificata da https://www.salute.gov.it/imgs/C_17_pubblicazioni_2696_allegato.pdf

Considerazioni da effettuare al momento dello switch

Drug Resistance:

- Review ART history for possible VF
- Review all available resistance test results
- If earlier resistance uncertain, only consider switch if new regimen likely to maintain suppression of resistant virus
- Within-class switches usually maintain virologic suppression if no resistance to drugs in that class are present
- Caution when switching from boosted PI to another class if full treatment/resistance history not known
- Consult an expert when switching if resistance to ≥ 1 class

Safety:

- Review ART history for intolerance
- Must be HLA-B*5701 negative if considering ABC
- Consider drug–drug interactions with comedications

Comorbidity:

- HBV coinfection
- Cardiovascular disease or risk
- Renal function
- Bone mineral density
- Pregnancy
- Other coinfections

Modificata da DHHS ART Guidelines. December 2019.

Slide credit: clinicaloptions.com

- Il genotipo da solo non è sufficiente a predire i fallimenti virologici.

- Necessità di integrare parametri viro-immunologici del paziente e storia clinica del paziente.

- Introdurre «elementi nuovi» e più approfonditi per studiare il virus quali la viremia residua, l'HIV-DNA, il sottotipo e il genotipo storico

Algoritmo applicabile nella routine clinica che tiene conto di:

- Caratteristiche del ceppo virale (incluso il Sottotipo): Ciccullo et al. Odoacre dato a 5 anni
- Mutazione 184+TAM e genotipo storico: Borghetti et al. OFID
- Storia immunovirologica del paziente (Nadir CD4+ , tempo dalla diagnosi e di soppressione virologica)
- Condizioni attuali (HIV-RNA allo switch non rilevabile)
- HIV-DNA e parametri infiammatori

HIV-DNA predicts time to viral rebound during 3TC-DTG maintenance therapy

Materiali e metodi

- **Obiettivo**: valutare se livelli di HIV-DNA più alti al momento della semplificazione terapeutica si associano a rischio aumentato di fallimento virologico

- **Criteri di inclusione**:
  - Pazienti adulti, HIV+
  - Virologicamente soppressi (HIV-RNA<37 cp/mL)
  - Switch a 3TC-DTG
  - HBsAg-negativi

- **Analisi statistica**: regressione multivariata di Cox per definire il ruolo di HIV-DNA basale (variabile dipendente) sul tempo al rebound virologico (= prima determinazione di HIV-RNA> 37 cp/mL), dopo aggiustamento per possibili confondenti

Caratteristiche della popolazione al baseline

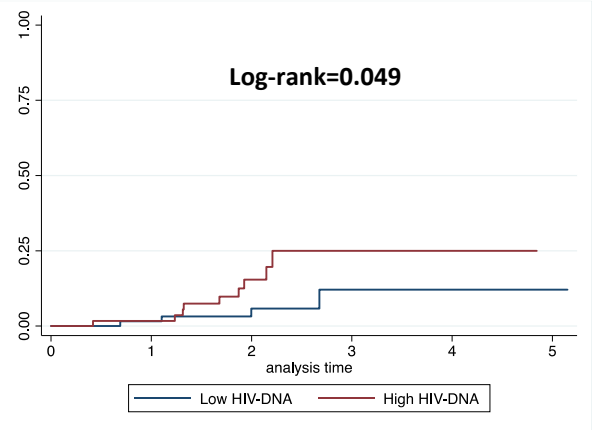
Variabili	N=124
Età (anni)*	**53 (43-59)**
Sesso maschile	**88 (71.0)**
Etnia: **- caucasico** **- non caucasico**	 **114 (91.9)** **10 (8.1)**
Fattore di rischio per HIV: **- Etero** **- MSM** **- IDU** **- Altro/ignoto**	 **53 (42.8)** **64 (51.6)** **5 (4.0)** **2 (1.6)**
Anti-HCV positivi	**8 (6.5)**
Stadio CDC C	**35 (28.2)**
Sottotipo: **- B** **- non B** **- ignoto**	 **52 (42.0)** **16 (12.9)** **56 (45.1)**
Tempo dalla diagnosi (anni)*	**12 (6-21)**
Esposizione cumulativa ad antiretrovirali (anni)*	**10 (4-20)**
Anni soppressione*	**7 (3-12)**

Variabili	N=124
Fallimento precedente (almeno 1)	**53 (42.7)**
Fallimento INI precedenti	**3 (2.4)**
Nadir CD4 (cell/µL) *	**236 (115-381)**
CD4 al baseline (cell/µL) *	**719 (541-863)**
Zenith viremia (copie/mL) *	**59,046 (8,340-273,300)**
Rapporto CD4/CD8 al baseline	**0.90 (0.60-1.31)**
Terapie precedenti: **- 2NRTI+PI** **- 2NRTI+NNRTI** **- 2NRTI+INI** **- Dual**	 **10 (8.1)** **29 (23.4)** **67 (54.0)** **18 (14.5)**
Motivo stop precedente terapia: **- Semplificazione** **- Tossicità** **- Altro/ignoto**	 **99 (79.8)** **16 (12.9)** **9 (7.3)**
Log_{10} HIV-DNA copie/10^6 PBMCs*	**2.29 (2.01-2.49)**

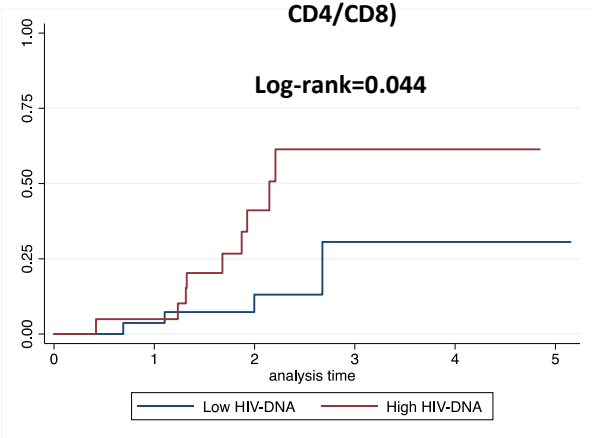
I numeri tra parantesi esprimono percentuali, tranne per le variabili continue* (range interquartile)

Analisi di sopravvivenza - Stime di Kaplan Meier

Analisi cruda



Analisi corretta per confondenti (sesso, età, etnia, anni di terapia, tempo di soppressione, CD4/CD8)



Probabilità di VF :

- **Low HIV-DNA**: 1.6% (95% CI 0.00-0.11) a 1 anno; 5.6% (95% CI 1.8-16.4) a 2 anni
- **High HIV-DNA**: 1.7% (95% CI 0.00-11.6) a 1 anno; 15.3% (95% CI 7.6-29.5) a 2 anni

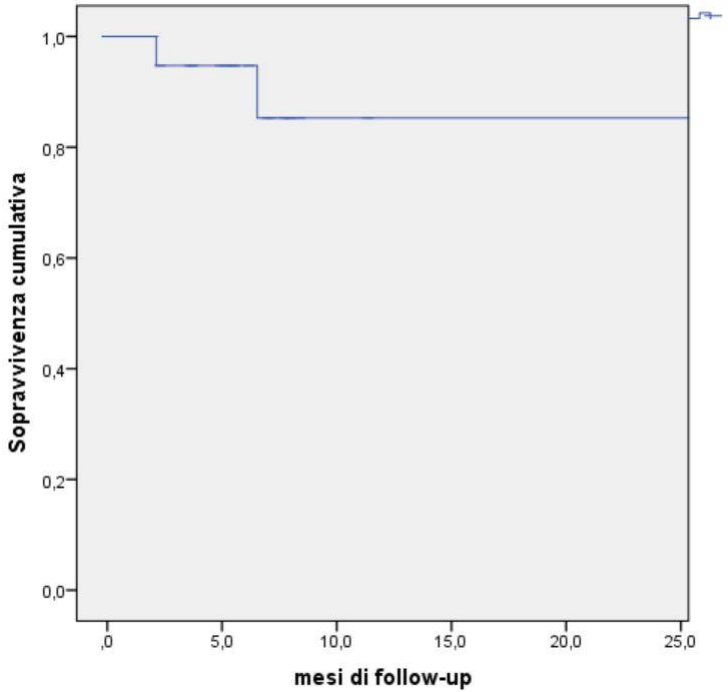
Real-life safety of doravirine in treatment-experienced, virologically suppressed PLWHIV

Ciccullo A, D'Angelillo A, Iannone V, Farinacci D, Lombardi F, Visconti E, Tamburrini E, Di Giambenedetto S

Variabili	N=36
Età, mediana (IQR)	52.5 (46.1 – 59.0)
Sesso maschile, n (%)	24 (66.7)
HIV risk factor: - Etero - MSM - IDU - Altro	 12 (33.3) 18 (50.0) 5 (13.9) 1 (2.8)
Anni di HIV, mediana (IQR)	11.0 (3.3 – 21.7)
Anni di ARV, mediana (IQR)	10.9 (3.3 – 18.0)
Pregresso evento AIDS, n (%)	14 (38.9)
Pregresso fallimento virologico, n (%)	8 (22.2)
HBsAg+, n (%)	3 (8.6)
Coinfezione HCV, n (%)	4 (11.8)
Nadir CD4+, mediana (IQR)	141 (43 - 275)
Zenith HIV-RNA, mediana (IQR)	5.29 (4.49 – 5.64)

Variabili	N=36
Pregresso uso RPV (storico)	28 (77.8)
Regime pre-switch: - 2NRTI+INI - 2NRTI+PI - 2NRTI+NNRTI - DTG+3TC - 4-drug - Naive	 12 (33.3) 8 (22.2) 11 (30.6) 1 (2.8) 1 (2.8) 3 (8.3)
Motivo start DOR: - Ottimizzazione - Tossicità - Naive - Altro	 27 (75.1) 3 (8.3) 3 (8.3) 3 (8.3)

Sopravvivenza del regime



Nella nostra analisi, a 12 mesi di follow-up, la probabilità di proseguire DOR è risultata pari a 85.3%

Sono state osservate 3 interruzioni durante 15.9 PYFU: una per fallimento virologico e due per intolleranze gastrointestinali.

Resistenze

Al genotipo storico, 5 pazienti (13.9%) presentavano una resistenza maggiore agli NNRTI:

- 3 pazienti E138A
- 1 paziente K103N
- 1 paziente Y188L

Nessuno dei pazienti con mutazione agli NNRTI ha interrotto il regime con DOR né ha presentato rialzi di HIV-RNA.

Cardiovascular disease risk in a cohort of virologically-suppressed PLWHIV switching to doravirine: preliminary data from the real life.

Ciccullo et al. Submitted to AIDS

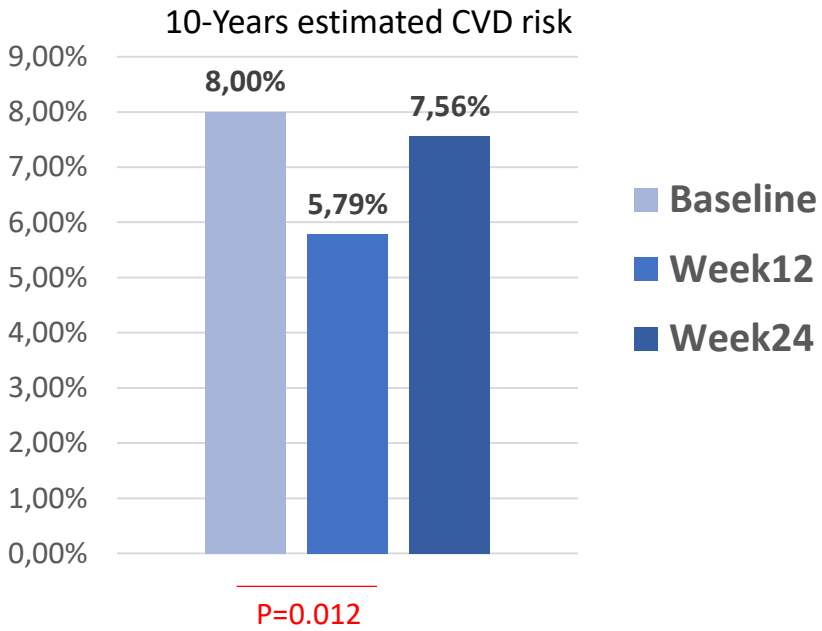
Background

- Doravirine (DOR), is a novel nonnucleoside reverse transcriptase inhibitor (NNRTI) administered orally as a once-daily (QD) treatment for human immunodeficiency virus infection in treatment naive adults.
- Clinical trials and clinical-practice studies have shown the efficacy of a 3-drug regimen with DOR plus 2 nucleot(s)ide reverse-transcriptase inhibitors (NRTIs) for the treatment of both naïve and experienced people living with HIV (PLWHIV), while also highlighting its favorable metabolic profile and neutral effect on weight of DOR [3,9].
- Aim of this study is to assess the impact of DOR-based regimens on cardiovascular risk in treatment-experienced PLWHIV.

Variables	N=40
Age, median (IQR)	54 (48-60)
Male sex, n (%)	25 (62.5)
HIV risk factor: - Heterosexual - MSM - IDU	 15 (37.5) 19 (47.5) 6 (15.0)
Years of HIV infection, median (IQR)	11.1 (5.8-20.2)
Years of ARV exposure, median (IQR)	11.0 (5.4-17.9)
CDC Stage C, n (%)	14 (35.0)
Previous virological failure, n (%)	8 (20.0)
CD4+ cell count nadir, median (IQR)	131 (38-293)
Zenith HIV-RNA, median (IQR)	5.32 (4.60-5.66)
Pre-switch regimen: - 2NRTI + INI - 2NRTI + NNRTI - 2NRTI + PI - 2-drug regimen	 18 (45.0) 12 (30.0) 9 (22.5) 1 (2.5)
Active smokers, n (%)	23 (57.5)
Diabetes, n (%)	2 (5.0)
Hypertension, n (%)	6 (15.0)

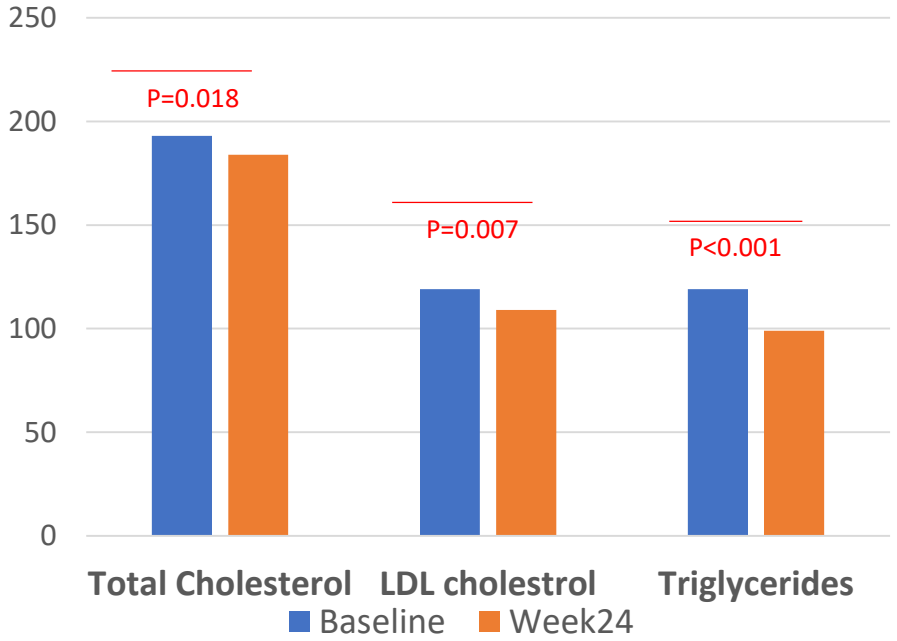
Results/1

At baseline, median predicted 10-year risk of cardiovascular disease (10Y-CD), estimated via Framingham risk score, was 8.0% (IQR 4.0-13.0). After 12 weeks, we observed a significant reduction in 10Y-CD (mean decrease -2.21, p=0.012); similarly, we observed a reduction at week 24, although not significant (mean -0.44, p=0.336). In our regression analysis, baseline 10Y-CD resulted the sole predictor of change after 12 weeks (per 1% more, -0.26, 95%CI -0.47 to -0.04, p=0.012).



Results/2

Regarding metabolic parameters, after 24 weeks we observed a significant reduction in total cholesterol (median change -8.8 mg/dL, p=0.018), LDL cholesterol (median -9.5 mg/dL, p=0.007) and triglycerides (median -19.8 mg/dL, p<0.001). Total cholesterol decrease was more pronounced in PLWHIV with a higher cholesterol determination at baseline (per 10 mg/mL more, -3.4, 95%CI -5.9 to -1.0, p=0.008) and in those coming from a INI or PI-based regimen compared to a NNRTI-based one (p=0.012). The reduction of LDL cholesterol was solely predicted by a higher LDL cholesterol value at baseline (per 10 mg/dL more, -4.0, 95%CI -6.4 to -1.7, p=0.002). Similarly, also the reduction in triglycerides was predicted by a higher value at baseline (per 10 mg/dL more, -8.1, 95%CI -8.5 to -7.7, p<0.001).



Conclusioni

- La triplice terapia resta essenziale in popolazioni difficili (IO, fallimento virologico, presenza di mutazioni archiviate)
- Le duplici terapie sono molto efficaci e supportate da trials e studi di pratica clinica consolidati e soprattutto il futuro si baserà su DT
- La terapia ARV non può essere Standardizzata ma deve essere sempre più possibile Personalizzata
- Sia le Triplice che la Dual sono approcci terapeutici fondamentali per «long-life treatment»
- Il futuro della terapia ARV saranno i LA e gli iniettivi…..siamo pronti?

A feasibility evaluation of long-acting cabotegravir-rilpivirine in clinical practice

D. Farinacci, S. Di Giambenedetto, A. Borghetti

Materials and methods

- **Objective**: to evaluate the proportion of HIV-positive patients eligible to switch to maintenance cabotegravir-rilpivirine according to clinical guidelines and patients' reported preferences.

- **Inclusion criteria**:
  - Adult patients (>=18 years)
  - Currently on combination antiretroviral therapy
  - With suppressed viral load (HIV-RNA< 50 cp/mL)

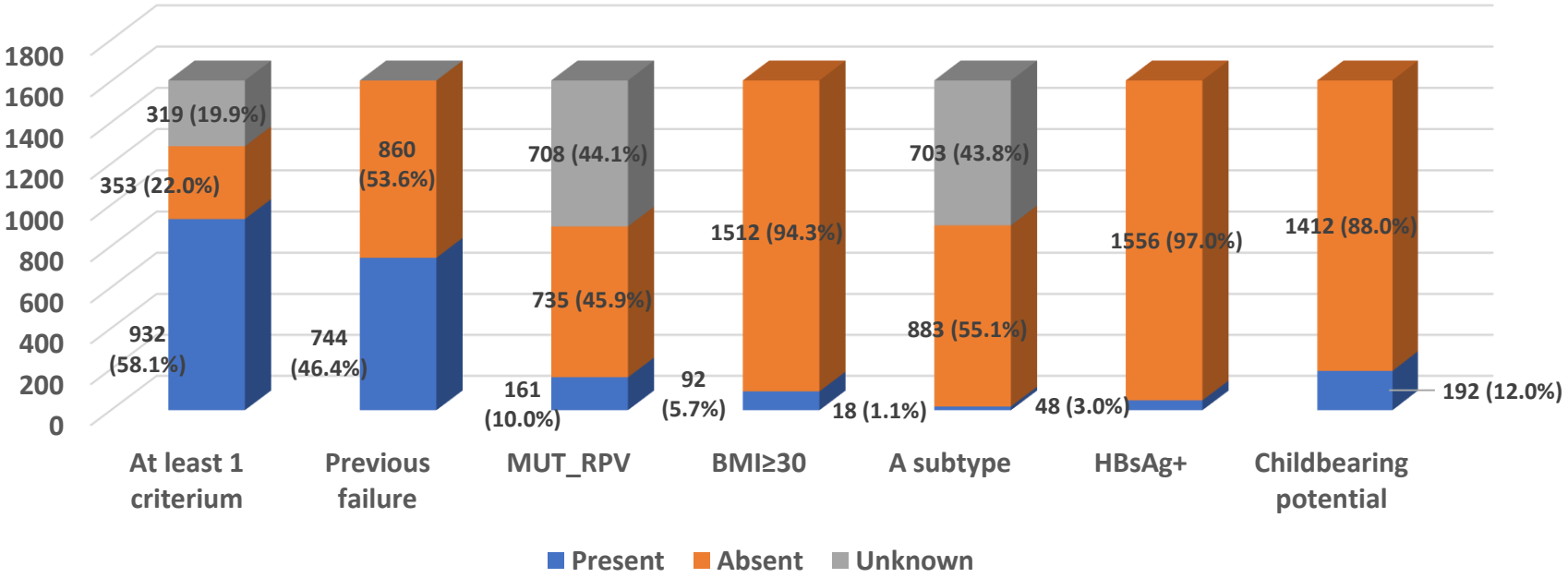
Caratteristiche della popolazione

Variables	N (%) = 1,604
Age (years)*	54 (46-60)
Male gender	1,091 (68.0)
Caucasian ethnicity	1,416 (88.3)
Mode of HIV transmission:	
- **Heterosexual**	678 (44.0)
- **MSM**	564 (36.6)
- **IDUs**	197 (12.8)
- **Other/unknown**	102 (6.6)
Anti-HCV positive serostatus	1,328 (82.8)
HBsAg-positive	1,556 (97.0)
CDC stage C	512 (31.9)
Time since HIV diagnosis (years)*	17 (9-24)
Cumulative time of antiretroviral therapy (years)*	14 (8-22)
Nadir CD4 count (cells/μL)*	192 (65-317)
Zenith HIV-RNA (log_{10} cp/mL)*	4.9 (4.2-5.4)
Time of viral suppression (years)*	9 (4-14)
Previous virological failure (at least one)	744 (46.4)
Number of therapeutic lines*	5 (4-8)
Current antiretroviral therapy:	
- **2 NRTIs + PI**	110 (6.8)
- **2 NRTIs + NNRTI**	388 (24.2)
- **2 NRTIs + INI**	612 (38.2)
- **3TC + PI**	45 (2.8)
- **3TC + DTG**	366 (22.8)
- **Other dual regimen**	83 (5.2)

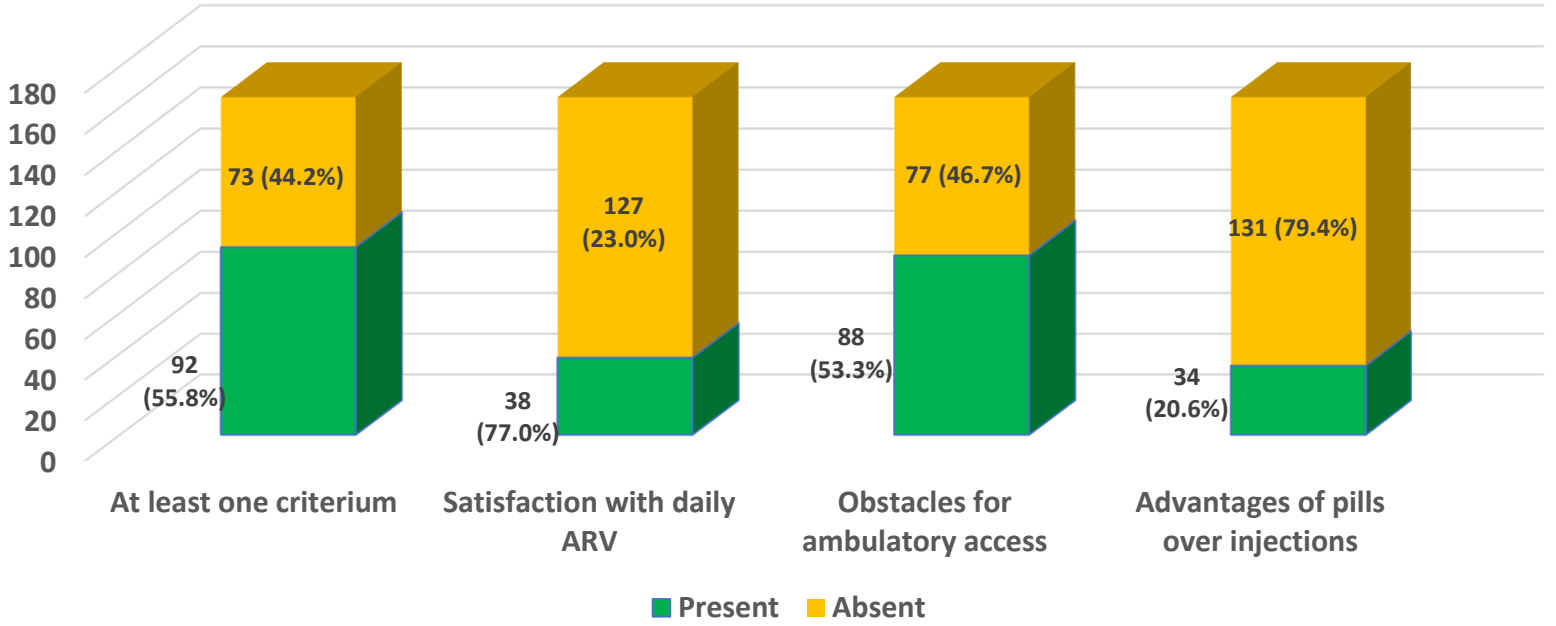
Caratteristiche della popolazione

Variables	N (%) = 1,604
Viral subtype:	
- **B**	731 (45.6)
- **A**	18 (1.1)
- **C**	50 (3.1)
- **CRF**	47 (2.9)
- **D**	1 (0.1)
- **F**	51 (3.2)
- **G**	3 (0.2)
- **Unknown**	703 (43.8)
Resistance-associated mutations to RPV:	N=896
- **At least one**	161 (18.0)
- **L100I**	9 (1.0)
- **K101E/P**	34 (3.8)
- **E138A/G/K/Q/R**	72 (8.0)
- **V179L**	1 (0.1)
- **Y181C/I/V**	44 (4.9)
- **Y188L**	17 (1.9)
- **H221Y**	17 (1.9)
- **F227C**	4 (0.5)
- **M230I/L**	8 (0.9)
Resistance-associated mutations to CAB:	N=18
- **At least one**	3 (16.7)
- **N155H**	2 (11.1)
- **R263K**	1 (5.6)

Clinical exclusion criteria from cabotegravir-rilpivirine

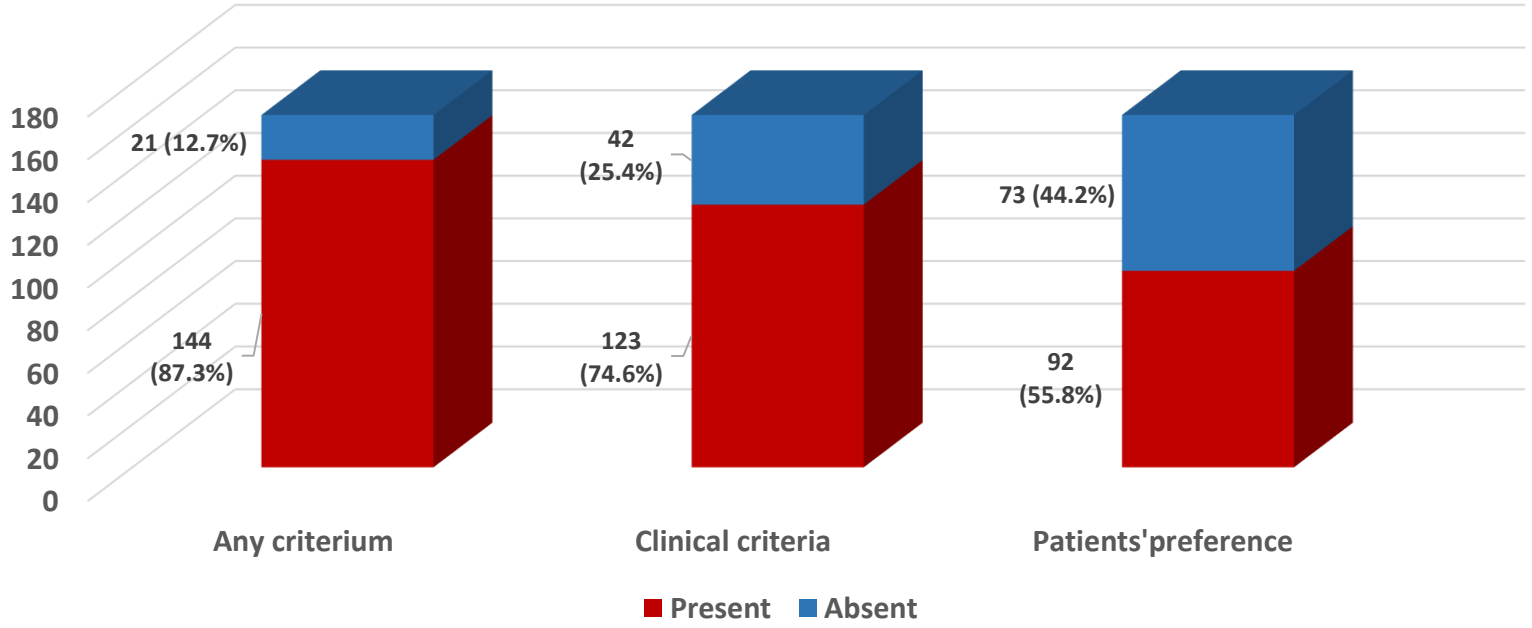


Patients' reported exclusion criteria



Satisfaction with daily ARV = Quanto ti piacerebbe l'idea di non assumere più farmaci per HIV tutti i giorni (0,1,2: nulla-moderata; 3,4,5: abbastanza-moltissimo)
Obstacles for ambulatory access = venire in ospedale per fare iniezione può essere un ostacolo (SI/NO)
Advantages for pills over injections = 0: preferenza per pastiglie su iniezioni; 1: preferenza di iniezioni su pastiglie

Exclusion from eligibility for any reason



Conclusions

- Overall, 22% of patients is eligible for a cabotegravir-rilpivirine dual therapy, based on clinical characteristics and according to International guidelines

- Considering patients’reported obstacles and preferences towards an injectable antiretroviral therapy, this proportion could be dramatically decreased in clinical practice

Grazie per l’attenzione