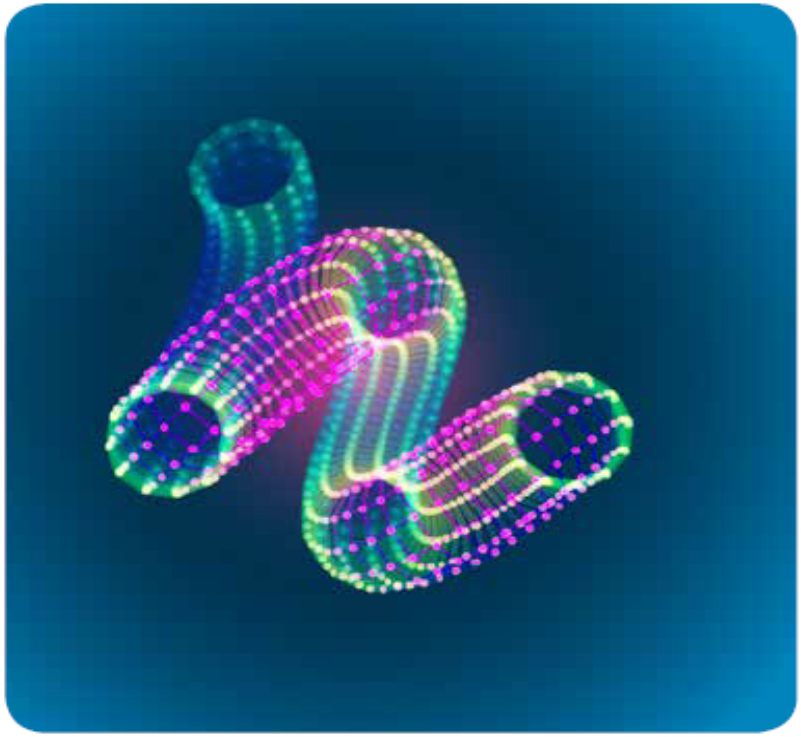


con il patrocinio di:

REGIONE DEL VENETO ULSS8 BERICA

Fondazione theBRIDGE SCIENZA TRA CLINICA E SOCIETÀ

VICENZA

AULA MAGNA ING. GRESELE
POLO UNIVERSITARIO ULSS 8 BERICA

CONTRÀ SAN BORTOLO 85

12 MARZO 2019

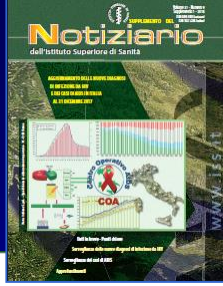
UPDATE HIV
NELLA REGIONE DEL VENETO

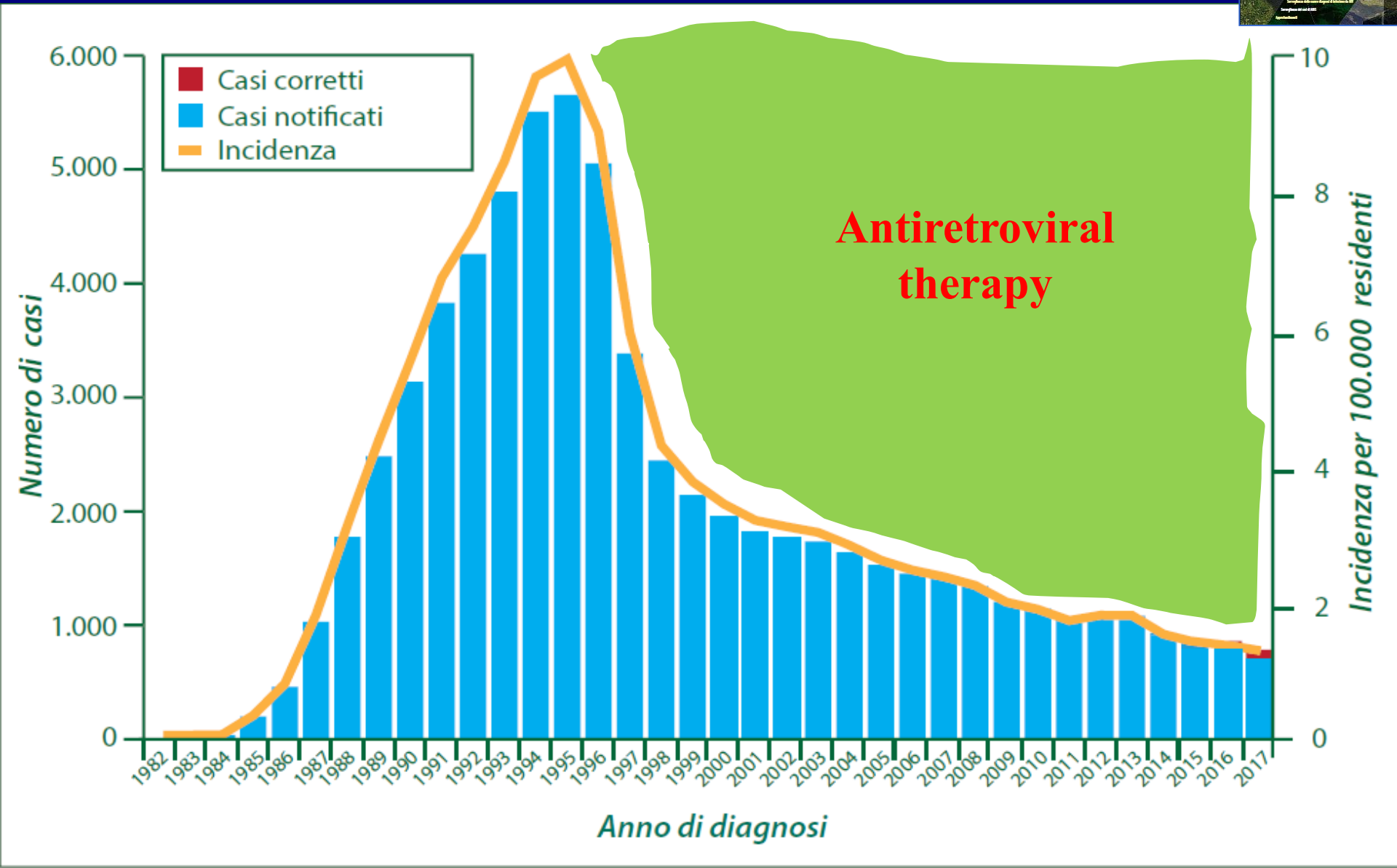
2019 MOTORE SANITÀ
Gestire il Cambiamento

Ottimizzazione della Terapia Antiretrovirale nei Pazienti in Soppressione Virologica

Anna Maria Cattelan

Numero dei casi di AIDS e incidenza per anno di diagnosi, (1982-2017)





Antiretroviral therapy in 2019

- Start ART at all CD4 cell counts
- 30 FDA approved drugs
  - -7 broad mechanistic classes: NRTI, NNRTI, PI, INSTI, a fusion inhibitor, a CCR5 antagonist, and a CD4 post-attachment inhibitor
- Up to 10 recommended first-line regimens
  - -1 standard strategy: 2 NRTI + (NNRTI, boosted PI, or INSTI)

ART Properties

Antiretroviral potency

Safety and Tolerability

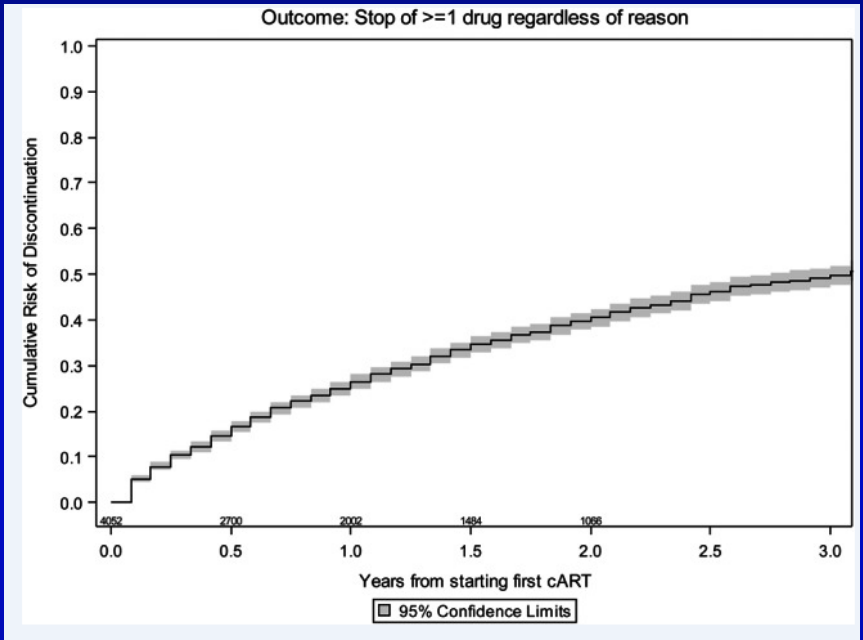
Convenience

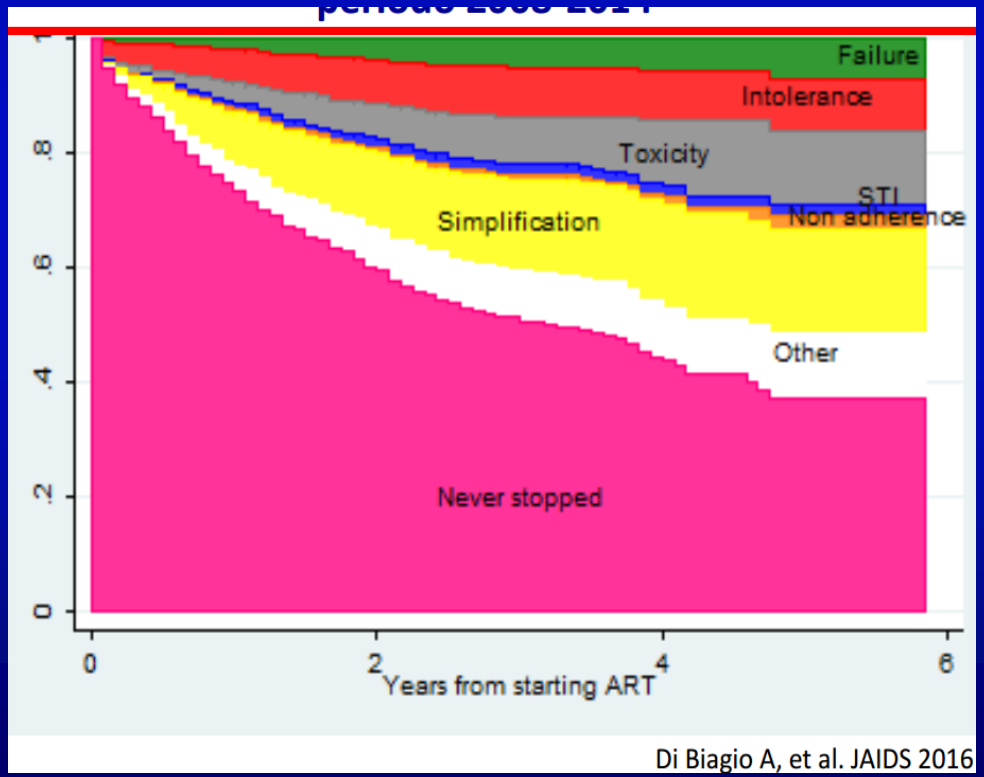
Life Expectancy

Goals of Antiretroviral Therapy in the long term follow-up

- Indefinitely maintain suppression of plasma HIV-RNA levels below the level of detection of sensitive HIV-RNA assays
- Minimize or eliminate short and long-term adverse effects of the therapy
- Prevent transmission of HIV-1 to others via <u>any route of exposure</u>

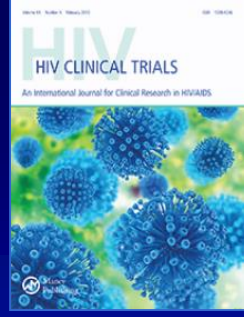
Cause di interruzione della prima linea HAART nel periodo 2008-2014 - ICONA





Di Biagio A, et al. JAIDS 2016

Durability and tolerability of first-line regimens including two nucleoside reverse transcriptase inhibitors and raltegravir or ritonavir boosted-atazanavir or -darunavir: data from the ICONA Cohort



ATV/r showed a 26% statistically significant higher risk of treatment failure (p = 0.001) compared to those initiating DRV/r. There was no evidence for a difference in treatment failure among participants starting RAL as compared to those starting DRV/r (p = 0.83)

All causes of discontinuation	ATV/r *N* = 627	DRV/r *N* = 605	RAL *N* = 125	Total *N* = 1357
Simplification	184 (29.4%)	276 (45.6%)	59 (47.2%)	519 (38.2%)
Toxicity	209 (33.3%)	124 (20.5%)	10 (8.0%)	343 (25.3%)
Other	70 (11.2%)	72 (11.9%)	11 (8.8%)	153 (11.3%)
Missing	38 (6.1%)	39 (6.5%)	9 (7.2%)	86 (6.3%)
Failure	50 (8.0%)	26 (4.3%)	7 (5.6%)	83 (6.1%)
Patient's decision	39 (6.2%)	23 (3.8%)	11 (8.8%)	73 (5.4%)
Clinical trial	14 (2.2%)	26 (4.3%)	11 (8.8%)	51 (3.8%)
Structured treatment interruption	18 (2.9%)	13 (2.2%)	6 (4.8%)	37 (2.7%)
Pregnancy	4 (0.6%)	4 (0.7%)	1 (0.8%)	9 (0.7%)
Death	1 (0.2%)	2 (0.3%)	0 (0.0%)	3 (0.2%)

D'Arminio Monforte A, et al. HIV Clin Trials 2018

OTTIMIZZAZIONE HAART
Definizione

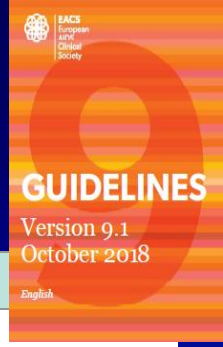
Il termine *ottimizzazione della ART* è utilizzato in queste linee guida per indicare strategie finalizzate alla miglior salute psico-fisica del paziente, attraverso modifiche al regime terapeutico in atto, con finalità differenti, ma sempre in condizioni di soppressione virologica (HIV-RNA <50 copie/mL).

Le principali finalità di un'ottimizzazione terapeutica sono:

- 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.

Linee Guida Italiane, 2017

Switch Strategies for Virologically Suppressed Persons



Class-sparing strategies

Dual therapy:

DTG + RPV
3TC + (DRV/r or DRV/c) or
3TC + (ATV/r or ATV/c)

In clinical trials these strategies have not been associated with more virological rebounds than triple therapy.

Monotherapy with DRV/r:

In clinical trials this strategy has been associated with more virological rebounds than triple therapy. DRV/r monotherapy is an option only for exceptional persons who are not candidates for dual therapies.

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months dual therapy with 3TC + PI/r or PI/c should only be given if there is a) no resistance and b) absence of chronic HBV co-infection. The same applies to DRV/r monotherapy.

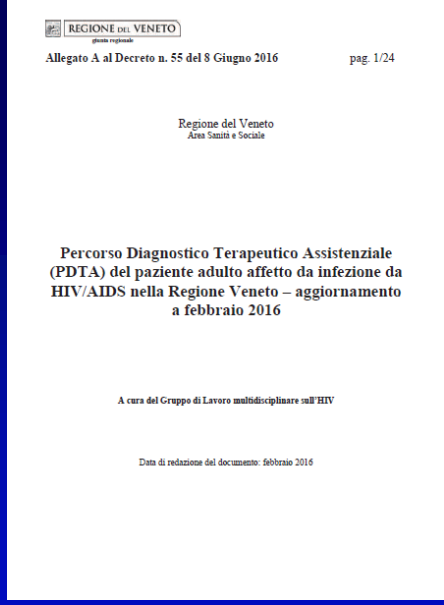
Strategies not recommended

a. Monotherapy with ATV/r
b. Monotherapy with DTG
c. Triple NRTIs combinations
d. Specific two-drug combination, i.e. 1 NRTI + 1 NNRTI or 1 NRTI + 1 unboosted PI, 1 NRTI + RAL, 2 NRTIs, MVC + RAL, PI/r or PI/c + MVC, ATV/r or ATV/c + RAL
e. Intermittent therapy, sequential or prolonged treatment interruptions

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression (Last updated October 25, 2018; last reviewed October 25, 2018)

Panel's Recommedations

- Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching an effective regimen to an alternative regimen in some situations.
- The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options **(AI)**.
- It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results, before selecting a new antiretroviral therapy regimen **(AI)**.
- Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch. Within-class and between-class switches can usually maintain viral suppression, provided that there is no viral resistance to the ARV agents in the new regimen **(AI)**.
- Monotherapy with either a boosted protease inhibitor or an integrase strand transfer inhibitor has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switching strategy **is not recommended (AI)**.
- When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, ARV drugs that are active against HBV infection should be continued. Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage.
- Consultation with an HIV specialist should be considered when planning a regimen switch for a patient with a history of resistance to one or more drug classes **(BIII)**.
- Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII)**.


REGIONE DEL VENETO
giunta regionale

Regione del Veneto
Area Sanità e Sociale

Percorso Diagnostico Terapeutico Assistenziale (PDTA) del paziente adulto affetto da infezione da HIV/AIDS nella Regione Veneto – aggiornamento a febbraio 2016

A cura del Gruppo di Lavoro multidisciplinare sull'HIV

Data di redazione del documento: febbraio 2016

Quesito 6: Come ottimizzare la terapia antiretrovirale nei pazienti in soppressione virologica?


REGIONE DEL VENETO
Allegato A al Decreto n. 55 del 8 Giugno 2016 pag. 1/24

Regione del Veneto
Area Sanità e Sociale

Percorso Diagnostico Terapeutico Assistenziale (PDTA) del paziente adulto affetto da infezione da HIV/AIDS nella Regione Veneto – aggiornamento a febbraio 2016

A cura del Gruppo di Lavoro multidisciplinare sull'HIV

Data di redazione del documento: febbraio 2016

Quesito 6: Come ottimizzare la terapia antiretrovirale nei pazienti in soppressione virologica?

Tabella 7: Raccomandazioni per l'ottimizzazione della terapia antiretrovirale nel paziente in soppressione virologica

Utilizzare la semplificazione verso regimi di comparabile o superiore efficacia, durevolezza e tollerabilità ma con costo inferiore rispetto al regime in atto. Tale strategia di semplificazione potrà essere proattiva e potrà essere condotta anche con l'obiettivo di ottenere un vantaggio in termini di costo-efficacia, rispettando comunque la validità scientifica della scelta.
Le strategie di semplificazione sono applicabili nei pazienti con soppressione virologica prolungata (HIV-RNA<50 copie/ml da più di 12 mesi) che non presentino controindicazioni o limitazioni in base alle strategie applicate.
Cambio da regimi con inibitori della proteasi boosterati (IP/ritonavir) a regimi contenenti inibitori non nucleosidici della trascrittasi inversa (NNRTI).
Cambio dal back-bone di tenofovir/emtricitabina ad abacavir/lamivudina (solo se HLA-B*5701 negativo).
Introduzione di regimi a formulazioni a dosi fisse per il miglioramento dell'aderenza specie in pazienti che utilizzano più farmaci insieme agli antiretrovirali.
Cambio da regimi a tre farmaci a regimi a due farmaci contenenti sempre un inibitore della proteasi boosterato(IP/ritonavir): a)atazanavir/ritonavir + lamivudina; darunavir/ritonavir+lamivudina o emtricitabina; lopinavir/ritonavir + lamivudina b) IP/ritonavir + inibitori non nucleosidici della trascrittasi inversa (NNRTI) c) darunavir/ritonavir o lopinavir/ritonavir + raltegravir.
Cambio da regimi a tre farmaci contenenti inibitori della proteasi boosterati (IP/ritonavir) o inibitori non nucleosidici della trascrittasi inversa (NNRTI) a regimi di monoterapia con inibitori della proteasi boosterati (darunavir/ritonavir o lopinavir/ritonavir).
Cambio verso regimi a incremento di costo solo nei casi di provata tossicità e/o intolleranza e assenza di strategie alternative.

PI monotherapy. First alternative approach to safe toxicities, reduce costs and increase semplicity

Study	N°	ART type	48-WK efficacy (Difference (%) of MT vs TT)*	VL>50 cp/ml	EA-related DC	% of DRM	Follow -up	N° pills
OK-04	102	LPV/r	85% (-5%)	6%	0%	2%	96 wks	4
MODAT	52	ATV/r	73% (-12%)	22%	4%	0%	96wks	2
MONET	127	DRV/r	84% (-1%)	9%	6%	<1%	96wks	2
PROTEA	137	DRV/r	86% (-9%)	NR**	4%	0%	96wks	2

***Differences in % of efficay at wk 48 by ITT of monotherapy minus standard therapy**
**** NR= not reported**

Why PI montherapy is not able to achieve similar rates of viral suppression than triple therapy?

- PI monotherapy seems to have higher level of immune activation
  - *Petrara et al. Plos One 2017; 12 (9): e0165128*
- PI monotherapy seems to achieve non-suppressive concentrations in the lymphonodes
  - *Fletcher et al. Proc Natl Acad Sci USA2014; 111(6): 2307-12*
- PI monotherapy is not given to the "right patient"
  - *Arribas et al. Hiv Med 2016; 17:358-67*

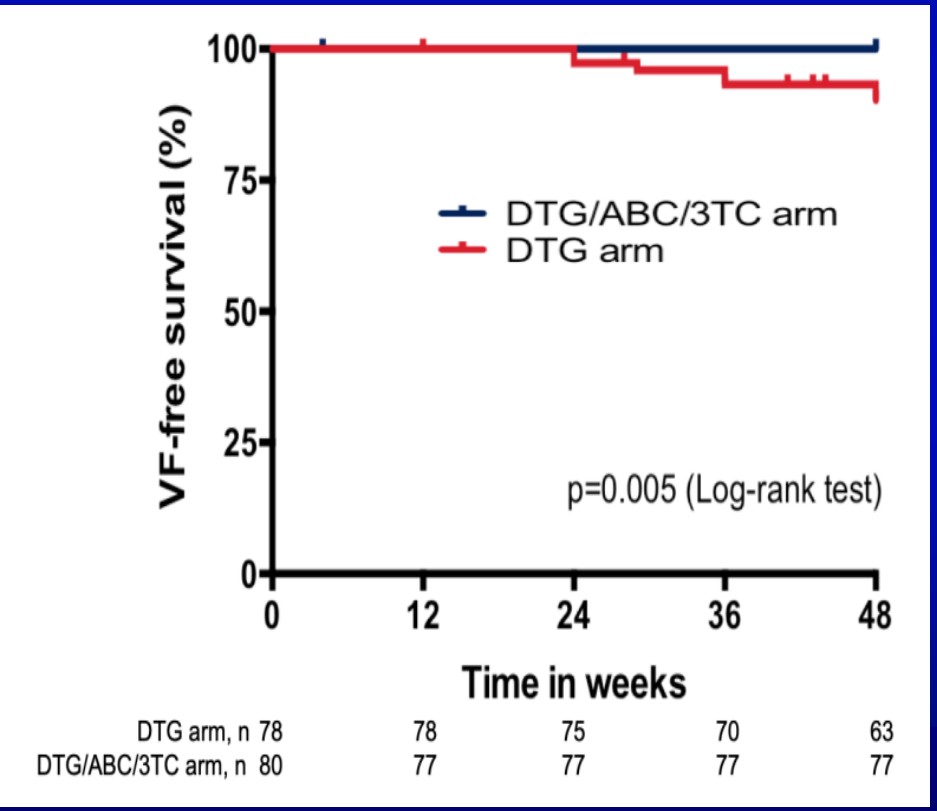
DTG monotherapy. A risk attempt of monotherapy, a great failure. Genetic barrier matters

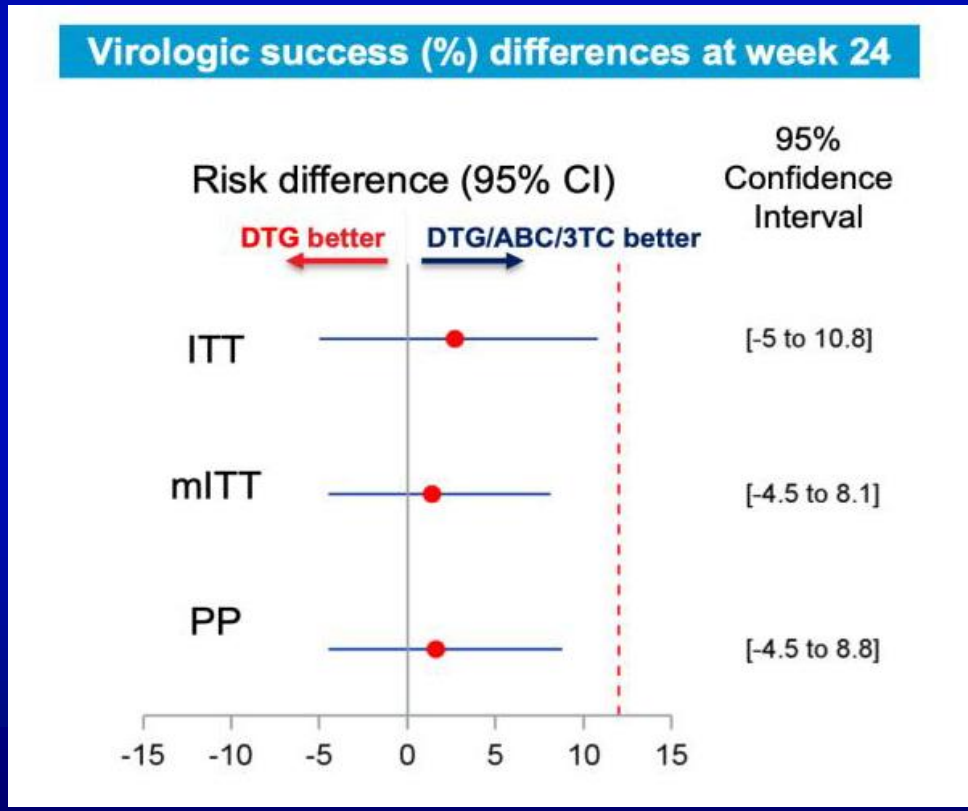
Study	N	Randomized study	Efficacy (Difference (%) of MT vs TT*	VL>50 cp/ml	EA-related DC	% of DRM	Follow-up
KATLAMA	28	NO	89%	11%	NR	11%	24 ws
REDOMO	122	NO	NR	9%	NR	7%	NR
DOLUMONO	96	Yes	92% (-6%)*	9%	NR	3% **	48ws

***compared with a cohort of 152 pts that continue conventional ART**
**** 155H, 263K and 230R**
NR= not reported

Dolutegravir monotherapy versus dolutegravir/abacavir/lamivudine for virologically suppressed people living with chronic HIV infection: the randomized non-inferiority MONCAY trial

Study design:48-week multicentric, randomized, open-label, 12% non-inferiority margin trial. Patients enrolled with CD4 nadir>100/µL, and HIV-1 RNA <50 for ≥12months





Hocqueloux L et al.CID, 2 January 2019 on line

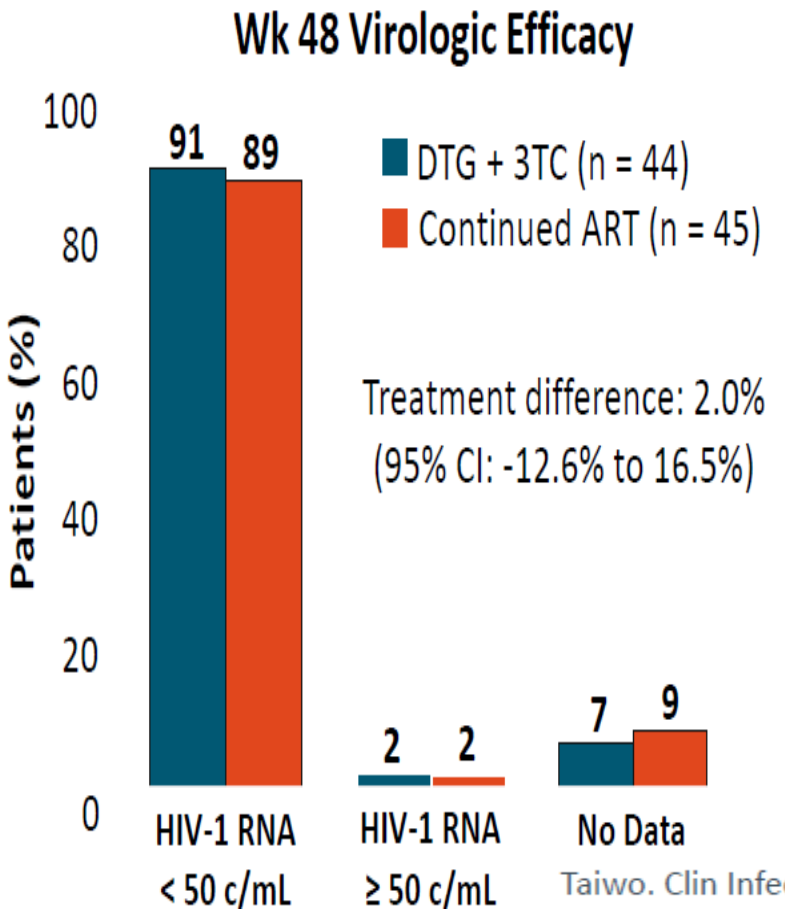
Dual therapies based on PIs: Aviremic patients

Study	N	ART Type	Efficacy Difference % of DT vs TT*	VL>50 cp/ml	EA-related DC	% of DRM	Follow-up	N° pills
OLE	121	LPV/r + 3TC	87% (-1%)	2%	3%	0%	48 wks	3-2
SALT	143	ATV/r + 3TC	83% (+6%)	6%	2%	0%	96 wks	3
ATLAS-M	133	ATV/r + 3TC	90%(+10%)	2%	3%	0%	48 wks	3
DUAL-GESIDA	126	DRV/r + 3TC	89%(-4%)	2%	<1%	0%	48 wks	3

***Differences in % of efficay at end of follow-u of PI + 3TC minus standard therapy control group**

ASPIRE: Switch to DTG + 3TC in Virologically Suppressed Patients on Triple ART

- Randomized, open-label, multicenter phase III trial in which virologically suppressed patients with no history of VF switched to DTG + 3TC QD or continued 3-drug ART (N = 90)



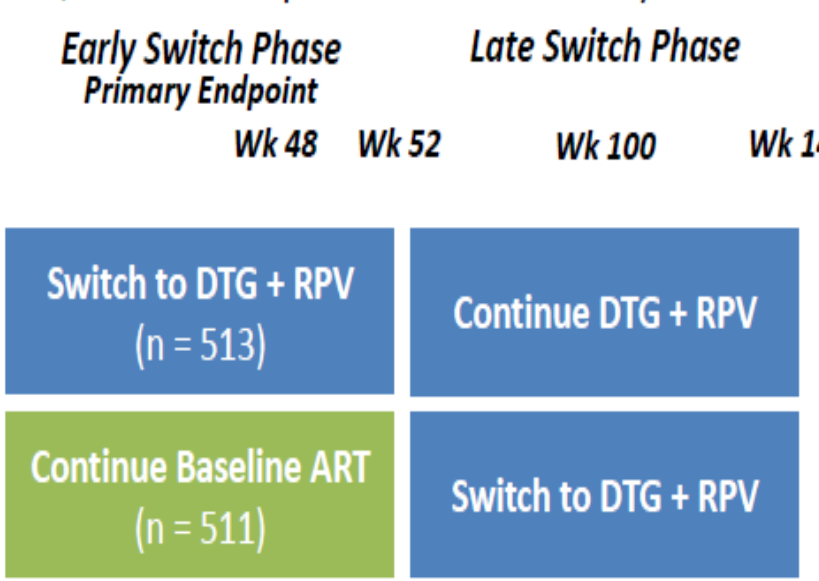
- Similar median changes from BL to Wk 48 in lipids (ie, TC, LDL, triglycerides) and CrCl between arms
- Similar rates of serious AEs between arms
- Discontinuation for AEs: n = 1 in DTG + 3TC arm, grade 2 constipation
- Phase III TANGO study ongoing comparing switch to DTG + 3TC vs continued ≥ 3-drug TAF-based ART in virologically suppressed patients

Taiwo. Clin Infect Dis. 2018;66:1794. Taiwo. EACS 2017. Abstr PE8/5. NCT03446573.

SWORD-1 and -2: Switch to DTG + RPV vs Continuation of Baseline ART in Virologically Suppressed Adults

- Parallel, randomized, open-label, multicenter phase III noninferiority studies[1]

Adults on stable ART (INSTI, NNRTI, or PI + 2 NRTIs*) with HIV-1 RNA < 50 copies/mL for ≥ 6 mos at screening; no previous VF or current HBV infection (N = 1024)



Virologic Response With DTG + RPV by FDA Snapshot (HIV-1 RNA < 50 copies/mL at Wk 100)[2]

89%

93%

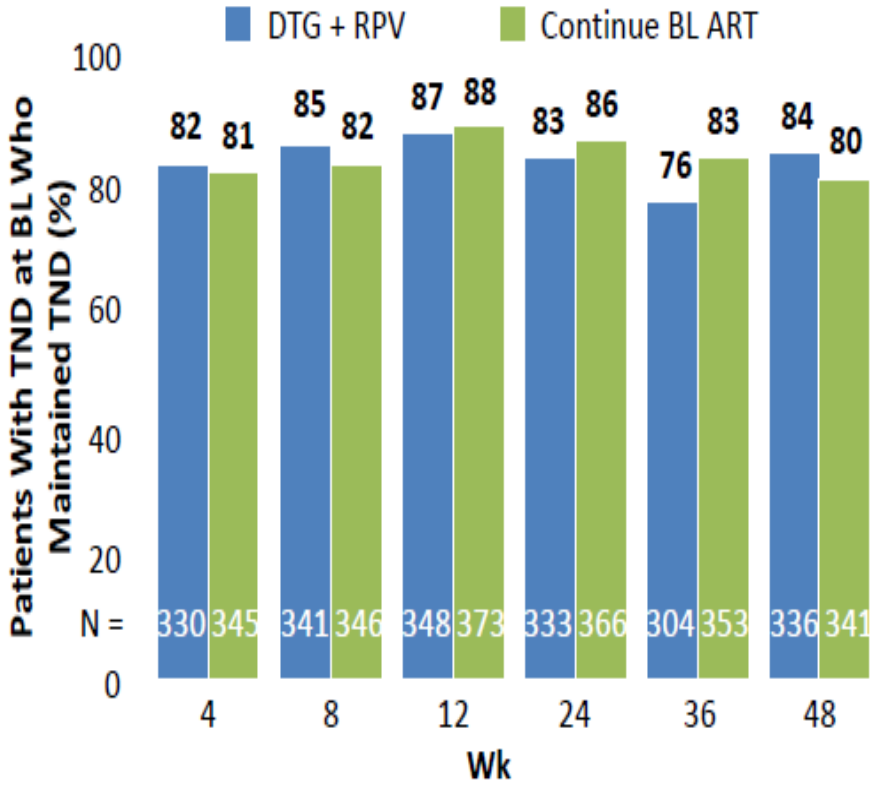
DTG dosed 50 mg PO QD; RPV dosed 25 mg PO QD.
*70% to 73% of patients receiving TDF at baseline.

- Primary endpoint: HIV-1 RNA < 50 copies/mL at Wk 48 (noninferiority margin: -8%)[3]
  - 95% in each arm at Wk 48 (adjusted treatment difference: -0.2%; 95% CI: -3.0% to 2.5%)
- Wk 100: 1% confirmed virologic withdrawal; emergent NNRTI resistance in 3/10, all early switch arm[2]

1. Underwood. Glasgow 2018. Abstr P311. 2. Aboud. AIDS 2018. Abstr THPEB047. 3. Llibre. Lancet. 2018;391:839.

SWORD-1 and -2: Viral Replication With HIV-1 RNA < 50 copies/mL

- Current analysis used viral load assay that reports qualitative target detected or target not detected for HIV-1 RNA < 40 copies/mL
- Patients with TND at baseline: 78% for DTG + RPV arm, 83% for continue BL ART arm

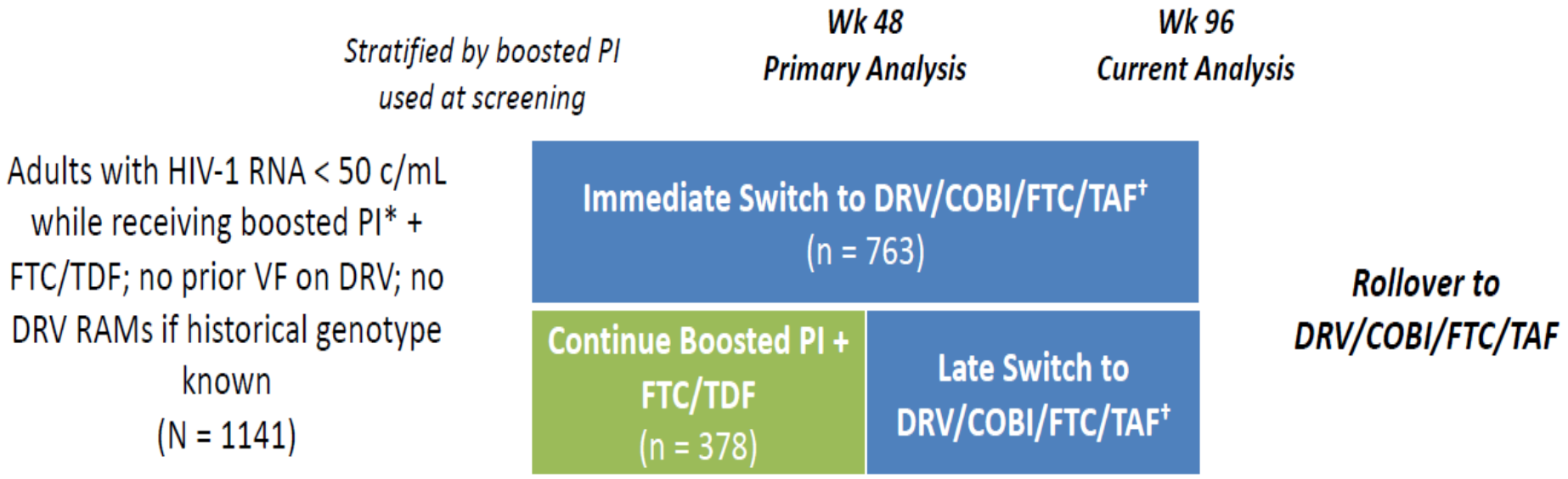


- Similar rate of post-BL TD and TND categories by BL category across arms
- Qualitative viremia by TD more common with BL TD vs BL TND
- No difference between arms in virologic success by TND at Wk 48 (FDA Snapshot)
  - DTG + RPV 84% vs continued BL ART 80% (adjusted difference: 3.1%; 95% CI: -2.2% to 8.3%)

Underwood. Glasgow 2018. Abstr P311.

EMERALD: Switch From Suppressive Boosted PI + FTC/TDF to DRV/COBI/FTC/TAF at Wk 96

- Multicenter, randomized, open-label phase III noninferiority trial

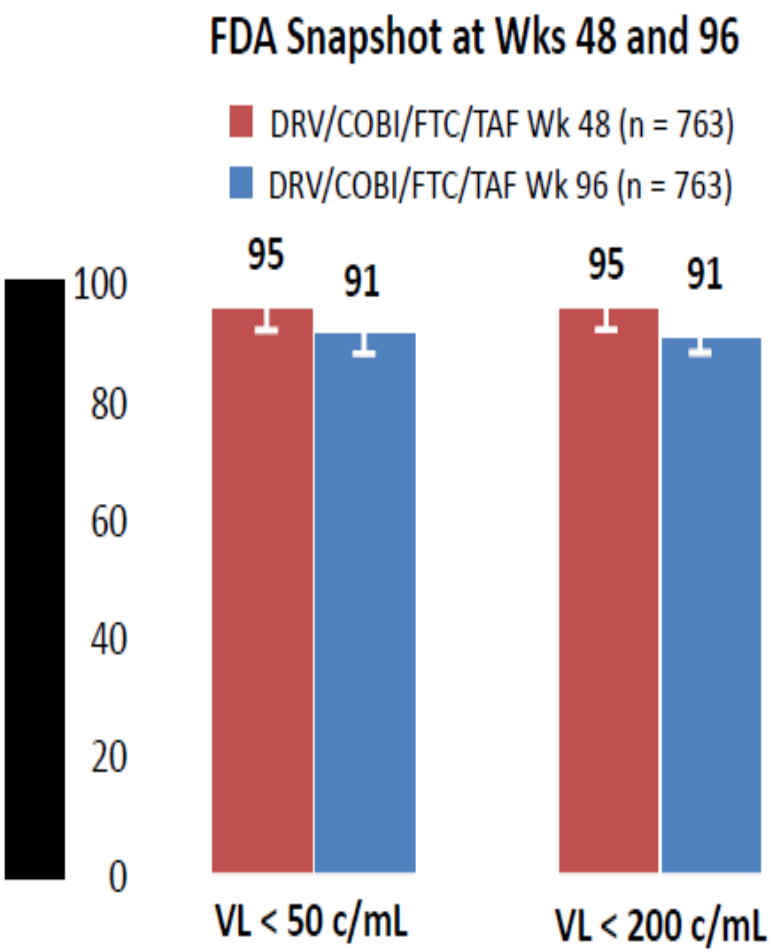


*Eligible boosted PIs: ATV/COBI or RTV, DRV/COBI or RTV, LPV/RTV. †800/150/200/10 mg QD.

- Primary endpoint: cumulative virologic rebound at Wk 48 (ITT)
  - Noninferiority margin: upper bound of 95% CI < 4%
  - **Switch to DRV/COBI/FTC/TAF** vs **continue boosted PI + FTC/TDF**: **2.5%** vs **2.1%** (difference: 0.4%; 95% CI: -1.5% to 2.2%; noninferiority *P* < .0001)

Eron. IDWeek 2018. Abstr 1768. Orkin. Lancet HIV. 2018;5:e23.

EMERALD: Virologic Outcomes in DRV/COBI/FTC/TAF Immediate Switch Arm Through Wk 96 (ITT)



*2-sided exact Clopper-Pearson 95% CI.

Cumulative PDVR	BL to Wk 48 (n = 763)	BL to Wk 96 (n = 763)
VL ≥ 50 c/mL, n (%) ▪ Rebounders resuppressed, n/N	19 (2.5) 12/19	24 (3.1) 14/24
VL ≥ 200 c/mL, n (%) ▪ Rebounders resuppressed, n/N	3 (0.4) 0/3	4 (0.5) 2/4

- No RAMs to DRV, tenofovir, or FTC and no primary PI RAMs observed post baseline

Eron. IDWeek 2018. Abstr 1768. Reproduced with permission.

EMERALD: Safety Outcomes in DRV/COBI/FTC/TAF Immediate Switch Arm Through Wk 96

- Low rates of study drug–related grade 3/4 or serious AEs, AE-related d/c (all ≤ 2%) maintained from Wk 48 to Wk 96
- No cases of subclinical proximal renal tubulopathy or Fanconi syndrome through Wk 96
- Lipid parameters stable from Wks 48 to 96
- Small (median change: ~ -1.0 mL/min) but statistically significant eGFR decrease from BL to Wk 96 ($P < .05$)

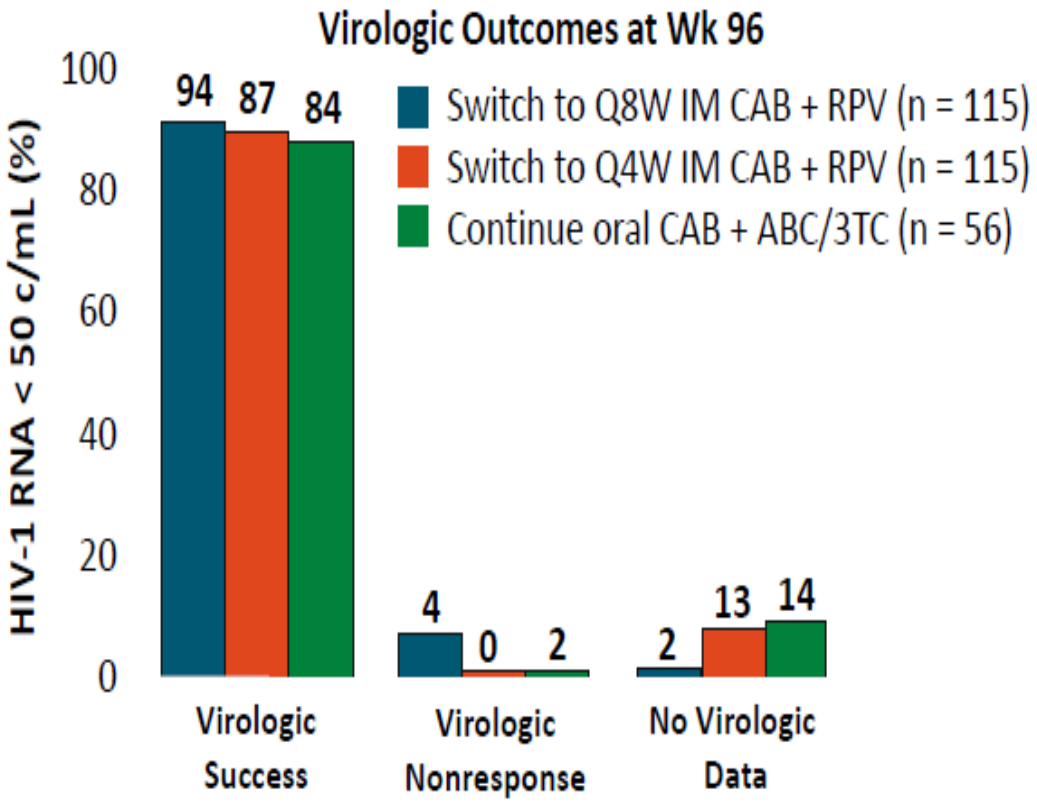
BMD Outcome	BL to Wk 48 (n = 164)	BL to Wk 96 (n = 173)
Mean percent change in hip BMD, %	1.49	1.85*
▪ Proportion with ≥ 3% increase	21	29
▪ Proportion with ≥ 3% decrease	2	3
Mean percent change in spine BMD, %	1.45	2.00*
▪ Proportion with ≥ 3% increase	31	37
▪ Proportion with ≥ 3% decrease	8	9

*$P < .001$ for within-arm change from BL by paired t-test.

Eron. IDWeek 2018. Abstr 1768.

LATTE-2: Induction With CAB + NRTIs Followed by Long-Acting CAB + RPV Maintenance

- Open-label, multicenter phase IIb study comparing continuation of oral CAB + ABC/3TC vs switching to IM CAB + RPV Q4W or Q8W (after induction with oral CAB + ABC/3TC)[1]



Treatment Difference vs CAB PO (95% CI)

CAB IM Q8W: 10.0% (-0.6% to 20.5%)

CAB IM Q4W: 3.0% (-8.4% to 14.4%)

Adherence to Dosing Window[2]

- 98% of injection visits occurred within 7 days of projected visit

1. Margolis. Lancet 2017;390:1499. 2. Sutton. AIDS 2018. Abstr THPEB084.

Ongoing Phase III Studies of Long-Acting CAB + RPV in Patients With Virologic Suppression

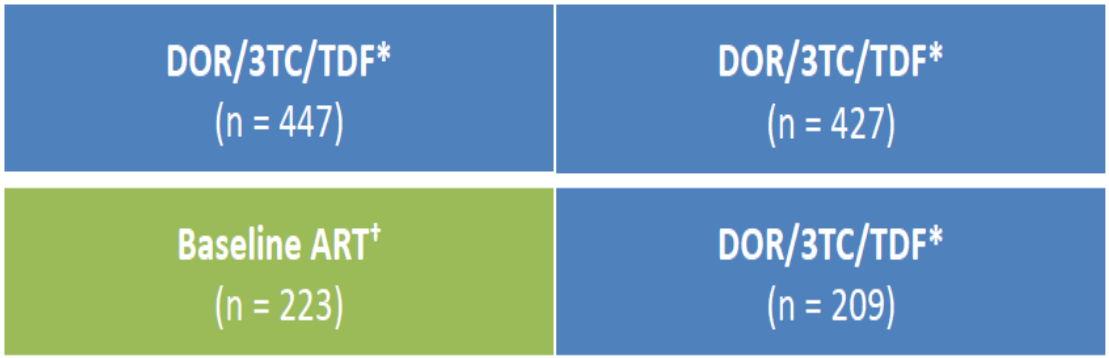
Study	Study Population	Switch Regimen
ATLAS[1]	▪ Patients on INSTI, NNRTI, or PI-based ART	CAB IM + RPV IM Q4W
FLAIR[2]	▪ Patients on DTG/ABC/3TC	CAB IM + RPV IM Q4W
ATLAS-2M[3]	▪ Patients on INSTI, NNRTI, or PI-based ART ▪ Patients from ATLAS	CAB IM + RPV IM Q4W or Q8W

1. NCT02951052. 2. NCT02938520. 3. NCT03299049.

DRIVE-SHIFT: Switch to DOR/3TC/TDF vs Continuation of Baseline ART in Virologically Suppressed Adults

- Multicenter, randomized, open-label phase III noninferiority trial

Adults with HIV-1 RNA < 40 copies/mL, stable ART for ≥ 6 mos with no prior virologic failure or resistance to study drugs, and eGFR ≥ 50 mL/min (N = 670)



*DOR/3TC/TDF dosing: 100/300/300 mg QD.

†2 NRTIs + RTV- or COBI-boosted PI (ATV, DRV, LPV), EVG/COBI, or NNRTI (EFV, NVP, RPV).

- Primary endpoint: HIV-1 RNA < 50 copies/mL (FDA Snapshot)
  - Noninferiority margin: lower bound of 95% CI > -8%
  - Time point comparisons: Wk 48 in immediate switch arm vs Wk 24 in baseline ART arm (primary); Wk 24 in each arm (secondary)

Kumar. IDWeek 2018. Abstr LB2.

DRIVE-SHIFT: Safety Outcomes Through Wk 48

- Switch to DOR/3TC/TDF associated with significantly greater decreases in LDL-C (-16.5 vs -1.9 mg/dL) and non–HDL-C (-24.7 vs -1.3 mg/dL) at Wk 24 vs continued BL ART in patients receiving PI/RTV-based ART at study entry (*P* < .0001 for both comparisons)

AEs, n (%)	Immediate Switch to DOR/3TC/TDF Wks 0-48 (n = 447)	Continued BL ART Wks 0-24 (n = 223)	Late Switch to DOR/3TC/TDF Wks 24-48 (n = 209)
Any AE	308 (68.9)	117 (52.5)	126 (60.3)
▪ Drug related	87 (19.5)	5 (2.2)	29 (13.9)
Serious AEs	13 (2.9)	8 (3.6)	4 (1.9)
▪ Drug related	2 (0.4)	0	1 (0.5)
D/c due to AE	11 (2.5)	1 (0.4)	4 (1.9)
▪ Drug related	7 (1.6)	0	4 (1.9)
Death	0	0	0

DRIVE-SHIFT: Efficacy of Switch to DOR/3TC/TDF at Wks 24 and 48 vs Continued BL ART at Wk 24 (FDA Snapshot)

Efficacy Analysis by FDA Snapshot, %	Immediate Switch to DOR/3TC/TDF (n = 447)	Continued BL ART (n = 223)	Difference Between Arms, % (95% CI)
Wk 24 DOR/3TC/TDF vs Wk 24 BL ART			
HIV-1 RNA < 50 copies/mL	93.7	94.6	-0.9 (-4.7 to 3.0)
HIV-1 RNA ≥ 50 copies/mL	1.8	1.8	0 (-2.3 to 2.3)
No virologic data	4.5	3.6	--
Wk 48 DOR/3TC/TDF vs Wk 24 BL ART			
HIV-1 RNA < 50 copies/mL	90.8	94.6	-3.8 (-7.9 to 0.3)
HIV-1 RNA ≥ 50 copies/mL	1.6	1.8	-0.2 (-2.5 to 2.1)
No virologic data	7.6	3.6	--

- No evidence of treatment-emergent resistance in patients receiving DOR/3TC/TDF

Kumar. IDWeek 2018. Abstr LB2.

HIV Neurological Disorders Can Occur in Patients With Suppressed HIV-1 VL in Plasma

CROI 2017 seattle

Poster number: 349

This retrospective multicenter study supported by the "Agence Nationale de Recherche sur le Sida et les Hépatites Virales" aims to evaluate a large population of antiretroviral treated patients who had a HIV RNA viral load (VL) >1.7 log_{10} copies/mL in CSF associated with cognitive impairment.

Characteristics	All Patients (n=227)	Patients with VL<1.7 log_{10} copies/mL in plasma (n=32)	Patients with VL>1.7 log_{10} copies/mL in plasma (n=195)	P-value
Age, years median (IQR)	45.1 (39.7-52.2)	47 (42-52)	45 (39-52)	P=0.229
Male, %	65,33	59,4	66,3	P=0.547
B subtype in CSF, %	54,3	59,4	53,3	P=0.570
B subtype in plasma, %	53,9	59,1	53,4	P=0.650
CSF HIV-1 RNA, log_{10} copies/mL median (IQR)	3.84 (3.13-4.57)	2.77 (2.05-3.34)	3.99 (3.29-4.69)	P<0.001
Plasma HIV-1 RNA, log_{10} copies/mL median (IQR)	3.34 (2.32-4.48)	1.6 (1.30-1.60)	3.70 (2.73-4.69)	P<0.001
Nadir CD4, cell count/mm^3 median (IQR)	67.5 (24-165)	92 (53-175)	63 (19-162)	P=0.064
CD4, cell count/mm^3 median (IQR)	230 (110-452)	476 (169-658)	214 (96-407)	P<0.001
Genotypic susceptible score	2	2	2	P=0.332
Charter Score	7,5	8,25	7,5	P=0.347

14% of patients with cognitive impairment and HIV RNA > 1.7 log10 copies/mL in CSF were well controlled in plasma. It is important to explore HIV CSF (VL and genotype) even if the HIV VL is controlled in plasma because HIV resistance could be observed. An optimization of antiretroviral treatment could be necessary using fully active drugs with improved central nervous system penetration

Do we still need non-standard ART?

YES

- **Some patients cannot receive conventional ART**
- **The less toxic drug is the one that you do not take**
- **Long actng combinations are needed in some patients**
- **Two drugs may be cheaper than three**

NO

- **Dual therapies may be not enough to fully control viral reservoirs**
- **Dual therapies may be associated with highr levels of immune activation**
- **Dual therapies may conditioning higher rates of senescence**

Key Clinical Questions in Switch Therapy

- Can 2-agent regimens be as effective as those with 3+ drugs for switch therapy?
  - Which regimens have the most compelling data?
- When/should generic agents be considered as part of combination therapy?
- Can the costs or toxicity of HIV treatment be reduced with these regimens?
- How do you approach patients who have stable viral suppression on an older ARV regimen?
- What should be the role of long-acting injectable therapy with CAB + RPV ?