Gestione del fallimento virologico durante terapia con LA

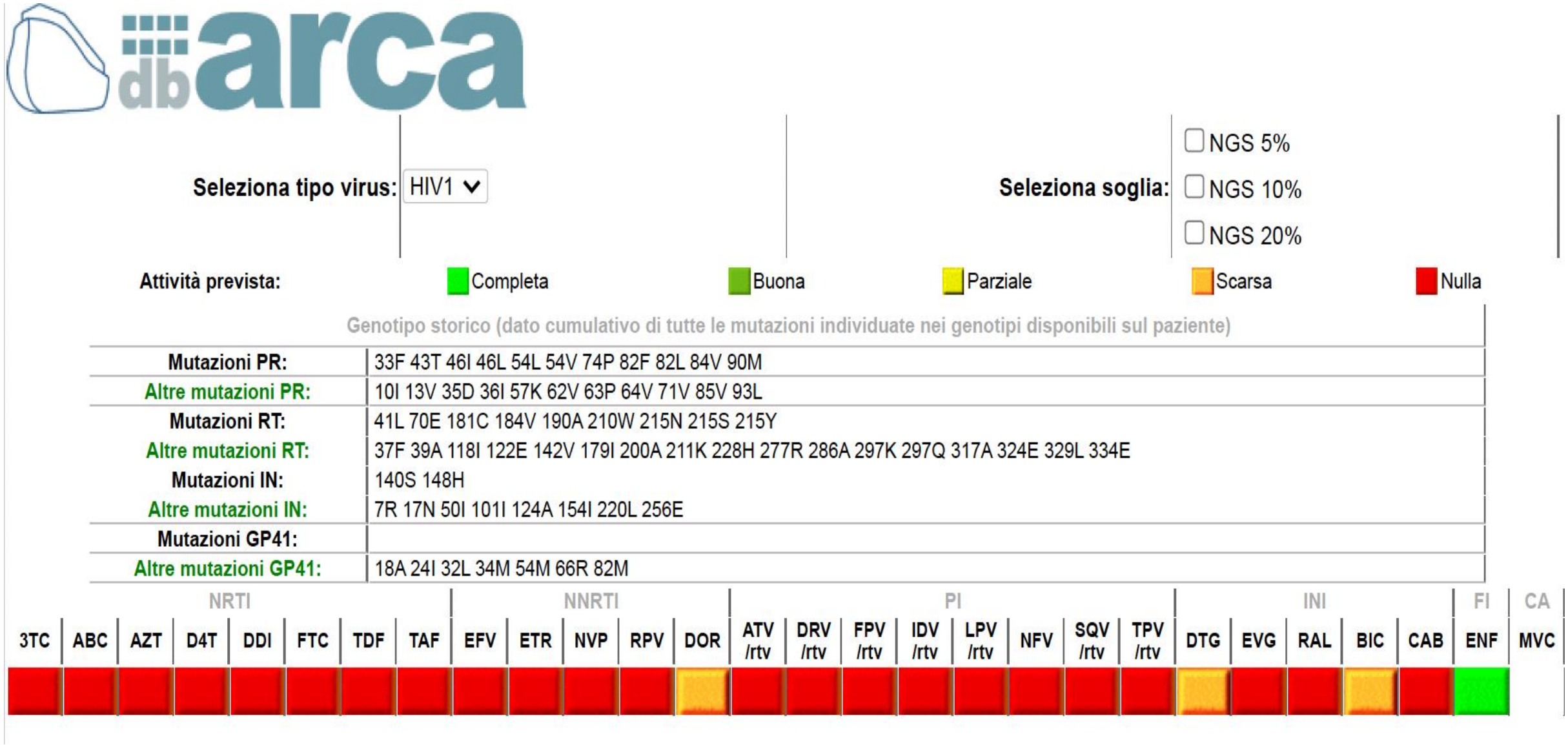
Antonio Di Biagio

Milano, 28 aprile 2025

Conflitti di interesse 2023-25

- **Attività di collaborazione: Janssen, MSD, Gilead, ViiV**
- **Fondi di ricerca per Ospedale per progetti: Gilead, ViiV**

Il Fallimento nei nostri database anche pre LA

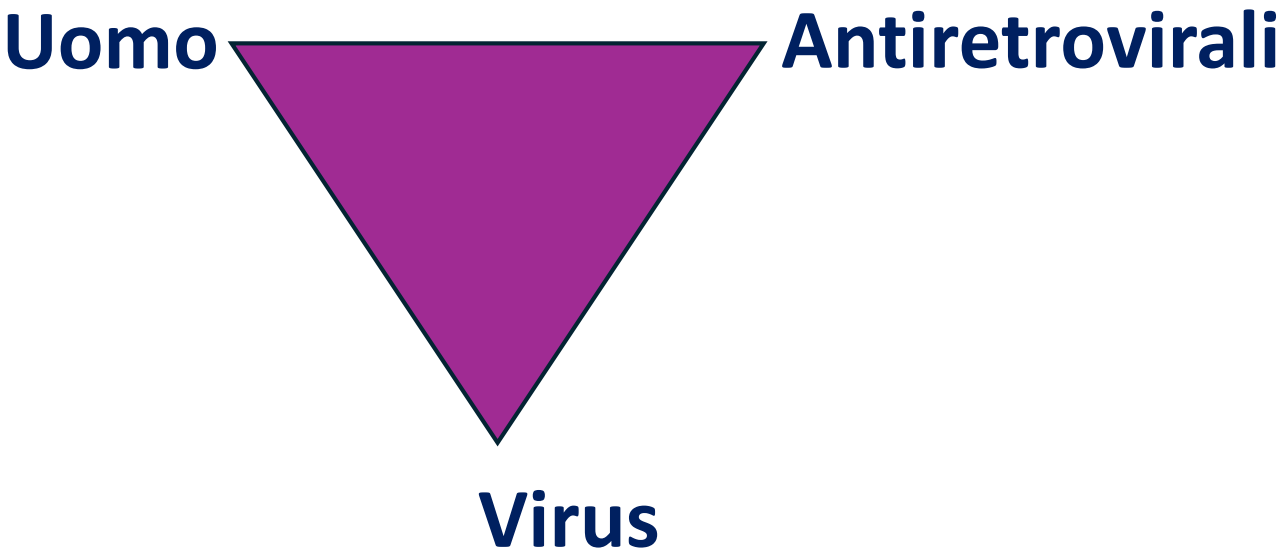


Il Fallimento ai LA nella nostra mente

The day after tomorrow

Una terapia antiretrovirale nasce dal ragionamento

Facile nel naive: bassa prevalenza mutazioni, cambio sce



Difficile nel fallimento (MDR, HTE)

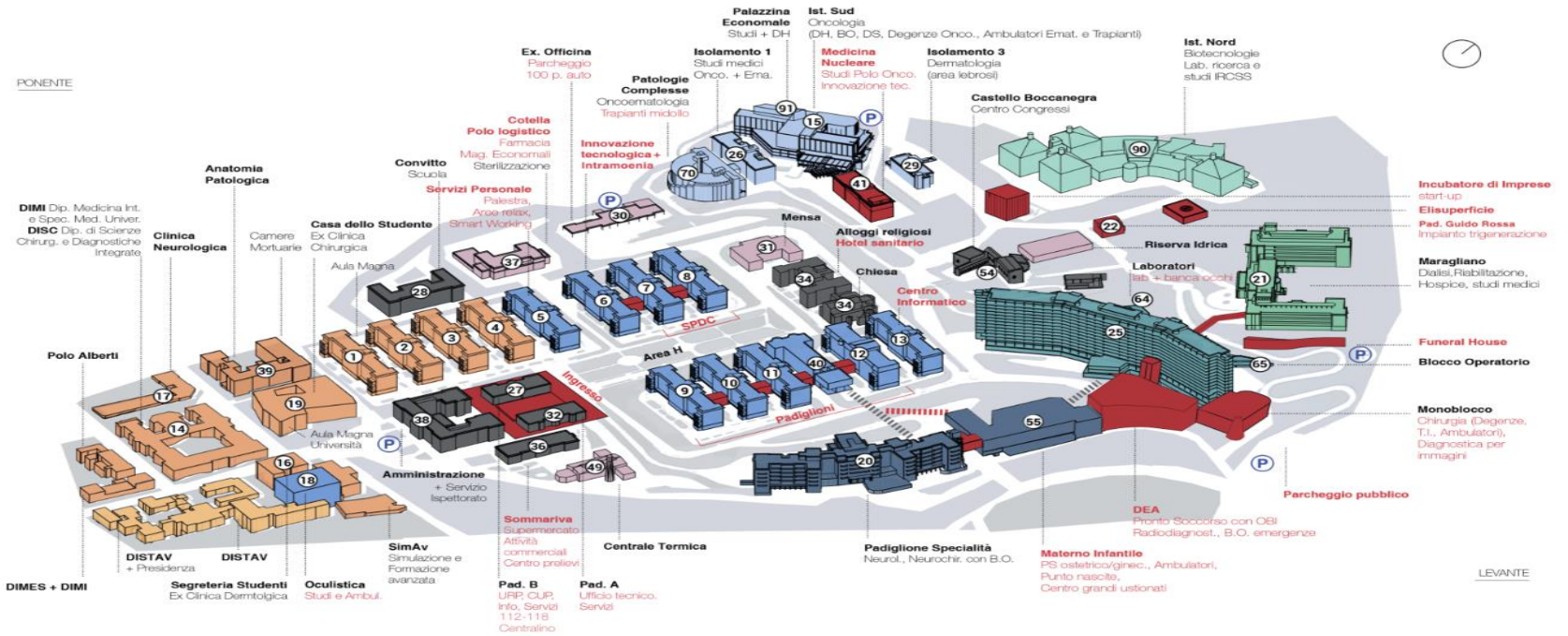
Difficile nello switch: se manca un GRT, storico, anamne

OSPEDALE POLICLINICO SAN MARTINO

Sistema Sanitario Regione Liguria

Istituto di Ricovero e Cura a Carattere Scientifico

1923 Cent'anni di cura 2023




. Agosto 1915 -

Park ospedale San Martino, Crivello: «Mesi per chiudere il buco»

- Il progetto, datato 1999, prevedeva un park da cinque piani per 420 posti auto. Lavori avviati nel 2007, che avrebbero dovuto concludersi nel 2010 per un costo totale di 10 milioni di euro e mai terminati.

assessore Crivello in consiglio
rtino

È stato per dieci anni uno dei buchi neri della città ma la vicenda del parcheggio di San Martino, davanti all'ingresso storico di largo Benzi

2023

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 00, Number 00, 2022

DOI: 10.1089/aid.2021.0161

Long-Term Effectiveness of Rilpivirine-Based Single-Tablet Regimens in a Seven-Year, Two-Center Observational Cohort of People Living with HIV

Lucia Taramasso,[1] Sergio Lo Caputo,[2] Laura Magnasco,[1] Federica Briano,[3] Mariacristina Poliseno,[2] Serena Rita Bruno,[2] Sergio Ferrara,[2] Rachele Pincino,[3] Giovanni Sarteschi,[3] Sabrina Beltramini,[4] Elisabetta Sasso,[4] Sara Mora,[5] Mauro Giacomini,[5] Matteo Bassetti,[3] and Antonio Di Biagio[3]

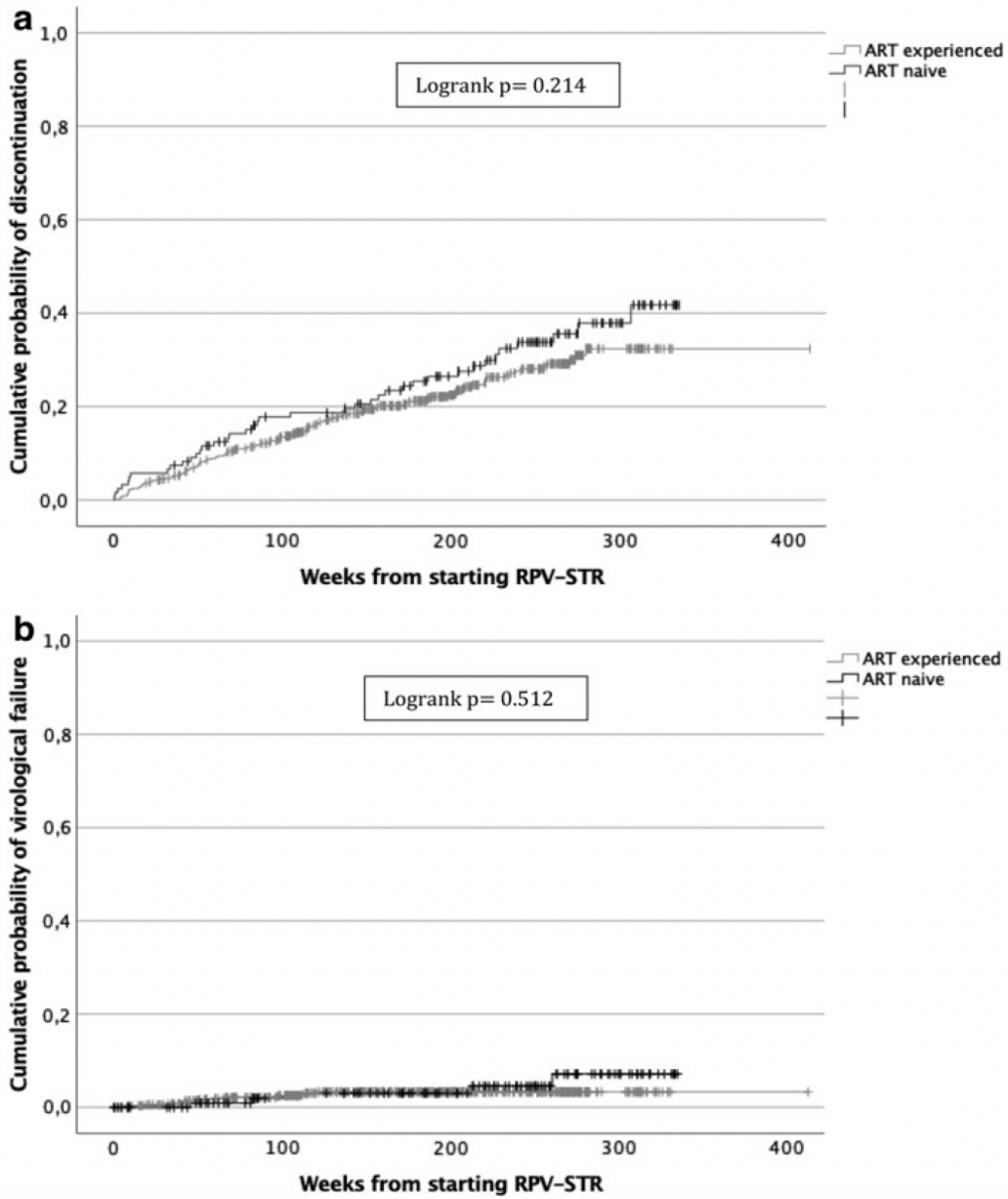


FIG. 1. Cumulative probability of RPV-STR discontinuation in ART-naïve and ART-experienced study participants due to any cause **(a)** and due to virological failure **(b)**. ART, antiretroviral therapy; RPV, rilpivirine; STR, single-tablet regimen.

Dove nascono i timori per i LA?

- **Insorgenza di fallimento (anche PWH con criteri d'entry)**
- **Ruolo delle pregressa storia clinica e virologica**
- **Difficile interpretazione dei test di seq. DNA**
- **Farmacocinetica ruolo non determinante**

Ripamonti et al. AIDS 20
Gutierrez et al. CID 202
Van Welzen, CID 2024
Thoveille, LHR 2024

A cautionary note on entry and exit strategies with long-acting cabotegravir and rilpivirine

Diego Ripamonti[a], Stefano Rusconi[b] and Maurizio Zazzi[c]

- undocumented failures in PWH with a complex treatment history. For example, PWH for longer than 25years were likely exposed to suboptimal therapy at a time when genotypic testing or even viral load testing was not universally available
- issue of missing data in PWH moving across different clinics
- failures without documented resistance , but testing may have not been performed at the right time (i.e. off medications)

«Obtaining drug resistance data from HIV DNA can be a barrier as most laboratories have long implemented RNA, but not DNA, analysis. However, we encourage HIV specialists not to skip this baseline analysis, as it may indeed detect RPV resistance"

AIDS 2024, **38**:263–265

Clinical Infectious Diseases

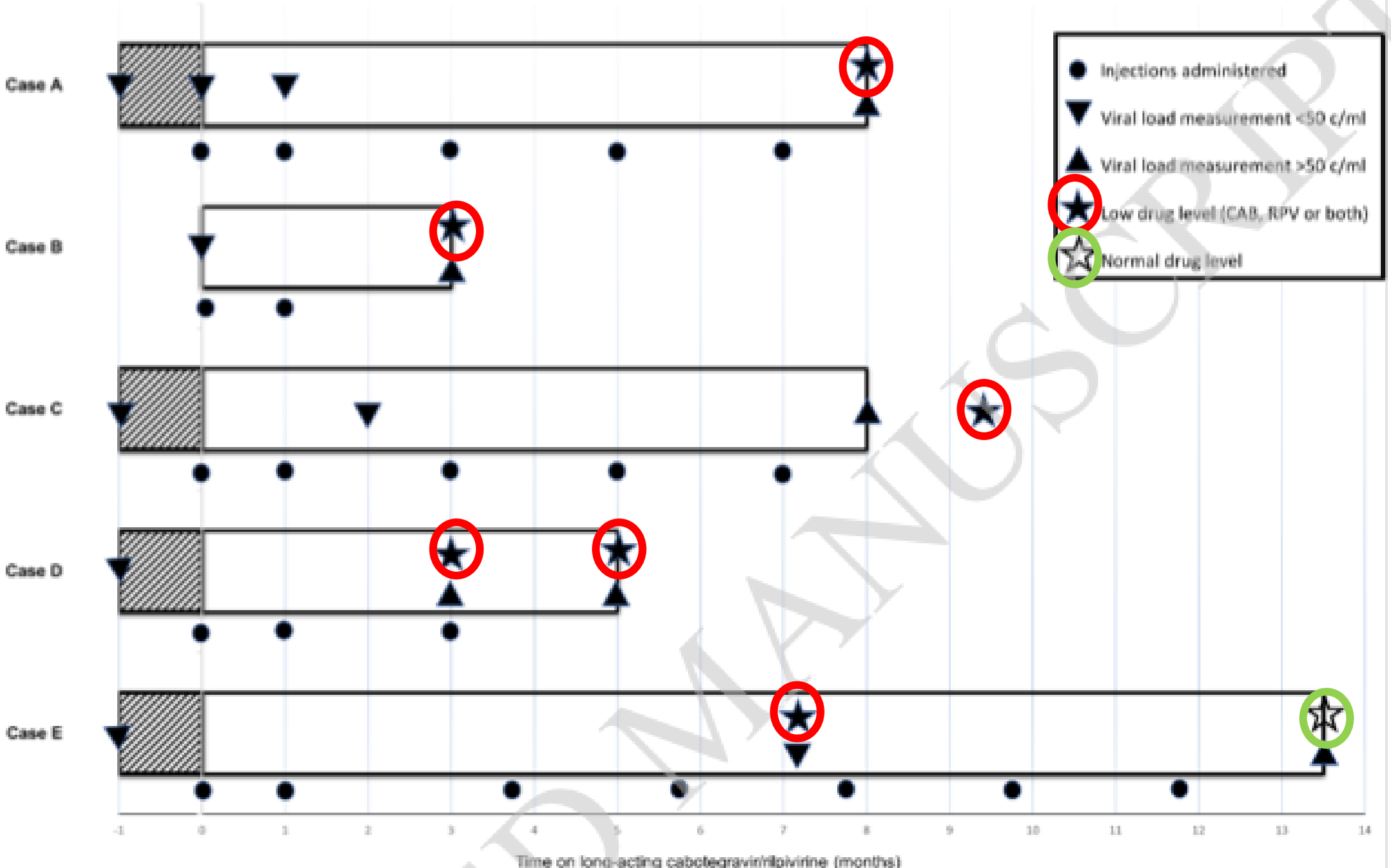
MAJOR ARTICLE

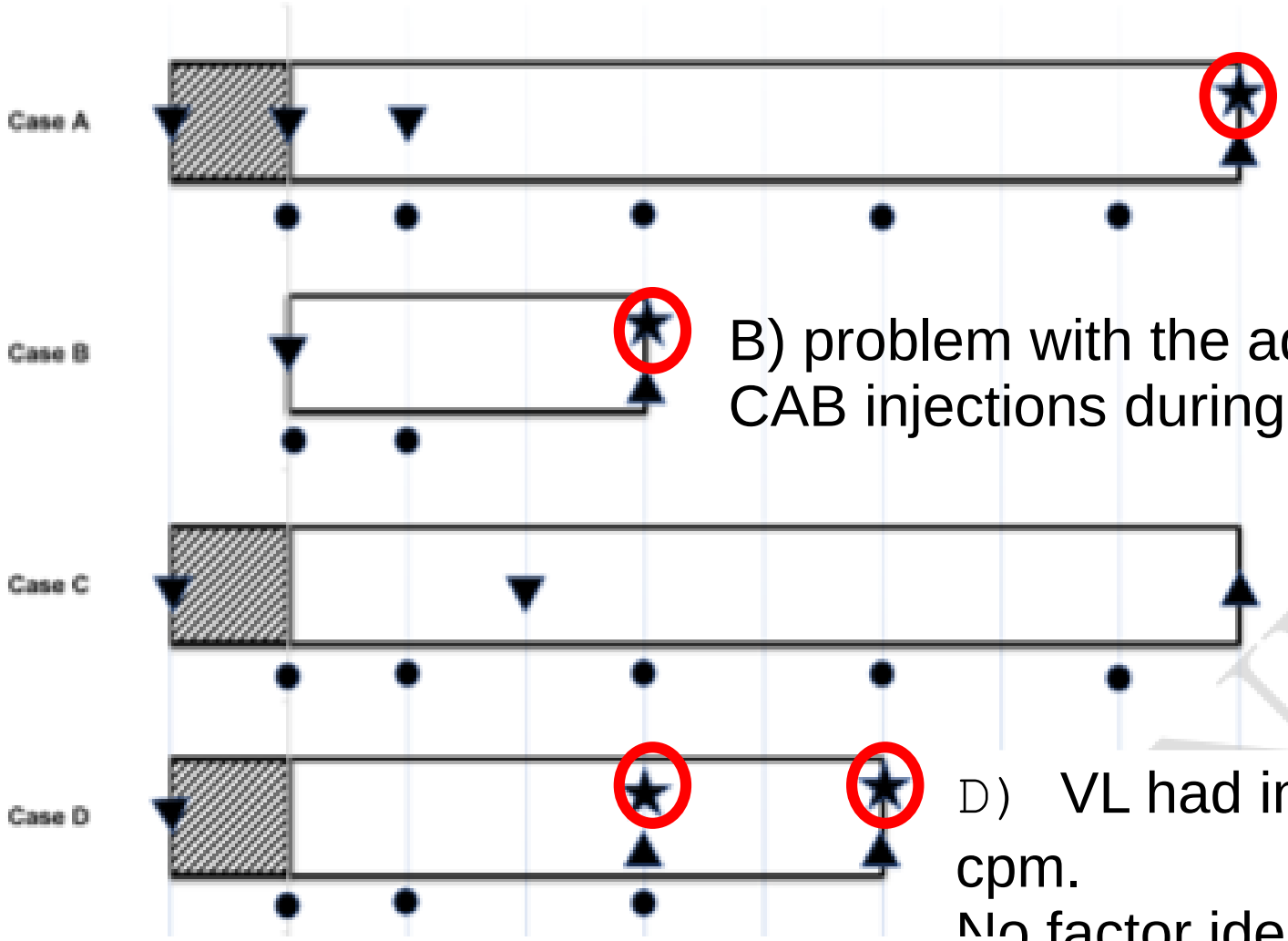
Virological failure after switch to long-acting cabotegravir and rilpivirine injectable therapy: an in-depth analysis

Berend J. VAN WELZEN MD PhD[1], Steven F.L. VAN LELYVELD MD PhD[2], Gerjanne TER BEEST MSc[3], Jet H. GISOLF MD PhD[3], Suzanne E. GEERLINGS MD PhD[4], Jan M. PRINS MD PhD[4], Gitte VAN TWILLERT MD[5], Cees VAN NIEUWKOOP MD PhD[6], Marc VAN DER VALK MD PhD[4,7], David BURGER PharmD PhD[8], Annemarie M.J. WENSING MD PhD[9,10]

in-depth clinical, virological and pharmacokinetic analysis on the reasons behind, and the impact of VF during LA CAB/RPV therapy in five cases from the Netherlands.
Genotypic resistance testing was performed after the occurrence of VF and drug plasma (trough) concentrations were measured after VF was established and on any other samples to assess on-treatment drug levels. CAB and RPV drug levels that were below the first quartile of the population cut-off (<Q1) were considered to be low.

Clin Infect Dis. 2024 Jan 11:ciae016.
doi: 10.1093/cid/ciae016. Online ahead of print.


Case A
Case B
Case C
Case D
Case E
Injections administered
Viral load measurement <50 c/ml
Viral load measurement >50 c/ml
Low drug level (CAB, RPV or both)
Normal drug level
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Time on long-acting cabotegravir/rilpivirine (months)



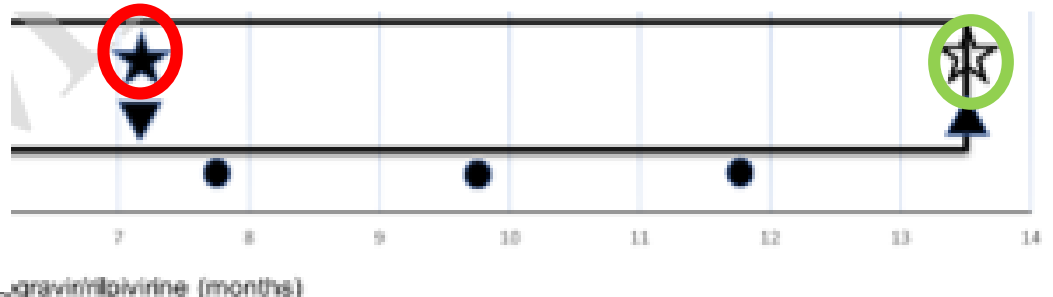
A) although BMI increased from 29.0 to 33.5 kg/m2 during the treatment course, the needle length was not adjusted.

B) problem with the administration of one of the CAB injections during the loading phase

C) BMI of 32 kg/m^{2}but needle length was not adjusted

D) VL had increased to 260 and 610000 cpm.
No factor identified

E) the third injection series was administered 11 weeks and two days after the second series due to a stay abroad. She did not use oral bridging to cover for



Real-world trough concentrations and effectiveness of long-acting cabotegravir and rilpivirine: a multicenter prospective observational study in Switzerland

Paul Thoueille,[a] Susana Alves Saldanha,[a] Fabian Schaller,[a] Eva Choong,[a] Aline Munting,[b] Matthias Cavassini,[b] Dominique Braun,[c,d] Huldrych F. Günthard,[c,d] Katharina Kusejko,[c,d] Bernard Surial,[e] Hansjakob Furrer,[e] Andri Rauch,[e] Mathieu Rougemont,[f] Pilar Ustero,[g] Alexandra Calmy,[g,h] Marcel Stöckle,[i] Catia Marzolini,[a,i,j] Caroline Di Benedetto,[k] Enos Bernasconi,[k,l] Patrick Schmid,[m] Rein Jan Piso,[n] Pascal Andre,[a] François R. Girardin,[a] Monia Guidi,[a,o,p] Thierry Buclin,[a] and Laurent A. Decosterd,[a,] on behalf of The Swiss HIV Cohort Study*

725 samples were obtained from 186 PWH

three experienced virologic failures (1·6%), of those, two had sub-optimal drug exposure. No association was found between low trough levels and detectable viral load.

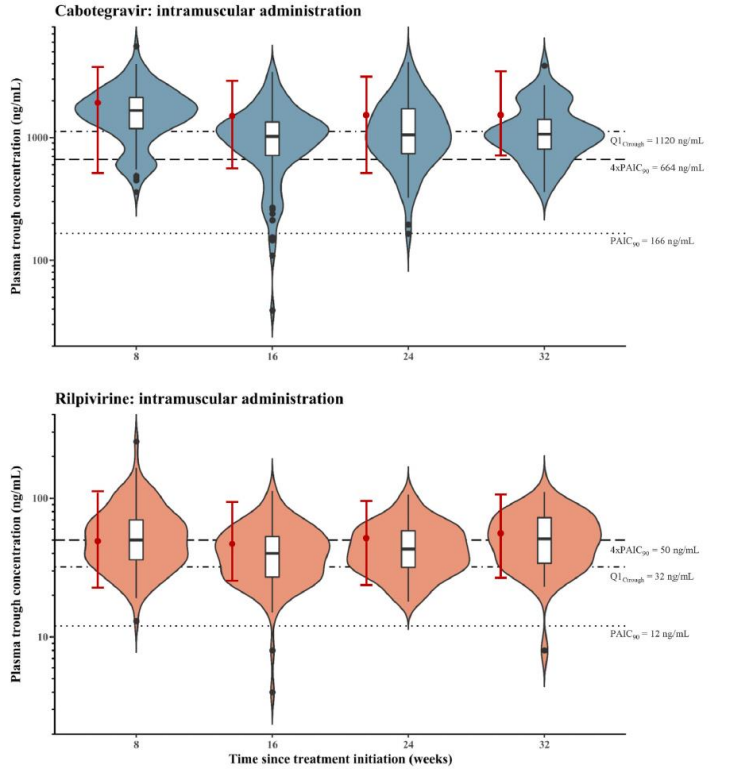


Fig. 2: Comparison of trough plasma concentrations of cabotegravir and rilpivirine over 32 weeks. The violin plots represent the distribution of concentration data. The boxplots depict the median and interquartile range. Whiskers extend from the lowest to the highest values comprised within 1.5 times the interquartile range. Outliers are represented by black dots. Concentration ranges from the ATLAS-2M trial are shown in red bars as medians (circles), 5% and 95% percentiles.[23] The horizontal lines correspond to the $PAIC_{90}$, $4xPAIC_{90}$ and $Q1_{Ctrough}$ thresholds reported.[4,7–9,12,13]

absorption in some PWH.

There is still no guidance for the interpretation of cabotegravir and rilpivirine therapeutic drug monitoring, yet various thresholds have been reported.[4,5,8,9,13]

CAB + RPV LA: TDM is not recommended in routine clinical practice

- TDM can be useful for drugs where there are no PK markers of therapeutic response and a consistent relationship between drug concentrations and optimal efficacy has been established[1]
  - In the case of CAB + RPV LA, efficacy can be easily and regularly monitored by virologic suppression[2,3]
  - Interpretation of an individual's CAB and RPV concentrations is difficult because the lower threshold of efficacy is not well-established due to low CVF rates with CAB + RPV LA[4]
- ≥2 BL risk factors (archived RPV RAMs, HIV-1 subtype A6/A1 and/or BMI ≥30 kg/m^2) can be used to inform patient selection for CAB + RPV LA[4]
  - Adding predicted CAB and RPV C_{trough}* to these BL factors did not enhance the predictive value for CVF
- Real-world studies have not shown TDM to be predictive of VF risk[5,6]
- The clinical utility of routine TDM with CAB + RPV LA is considered to be low, would be impractical in the majority of

*Model-predicted Week 4 $C_{troughs}$

C_{trough}, trough concentration

1. Buclin T, et al. Front Pharmacol 2020;11:177; 2. Ramgopal MN, et al. Lancet HIV 2023;10:e566–77
3. Kityo C, et al. Lancet Infect Dis 2024;24:1083–92; 4. Orkin C, et al. Clin Infect Dis 2023;77:1423–31
5. Thoueille P, et al. Lancet Reg Health Eur 2023:36:100793; 6. Seang S, et al. EACS 2023. Poster eP.B1.035
7. DHHS. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV, Sep 2024
8. EACS. Guidelines Version 12.1, Nov 2024

Cabotegravir plus rilpivirine injectable	Studied only in suppressed switch; high risk of NNRTI and INSTI resistance at virological failure

programme (GPP).

- We recommend the following viral load monitoring:
  - Two-monthly HIV RNA quantification (Grade 1A);
  - Prompt recall for repeat testing and resistance testing if viral rebound occurs (GPP).

Le certezze

CAB + RPV LA Q2M

High efficacy and a low rate of CVF has been demonstrated across a robust development programme

	ATLAS-2M	CARISEL (Protocol 213199)	SOLAR (Protocol 213500)	CARES
	N=522 (ITT-E)[1,2]	N=430 (ITT-E)[3]	N=447 (mITT-E#)[4]	N=255 (ITT-E)[5]
Virologically suppressed	**94%***	**87%§**	**90%§**	**96%***
CVF	**1.7%** (n=9) by Week 48†‡	**0.7%** (n=2) by Month 12‡¶	**0.4%** (n=2) by Month 12‡‖	**0.8%** (n=2) by Week 48‡#

Data up to 5 years from LATTE-2 exhibited long-term efficacy and tolerability, demonstrating the durability of CAB+RPV LA as a maintenance therapy[6]

2023;76:1646–54 (and suppl. appendix)
3. De Wit S, et al. IDWeek 2022. Oral 1584; **4.** Ramgopal MN, et al. Lancet HIV 2023;10:e566–77
5. Kityo C, et al. Lancet Infect Dis 2024 May 28;S1473-3099(24)00289-5;
6. Smith G, et al. Open Forum Infect Dis. 2021 Aug 25;8(9):ofab439

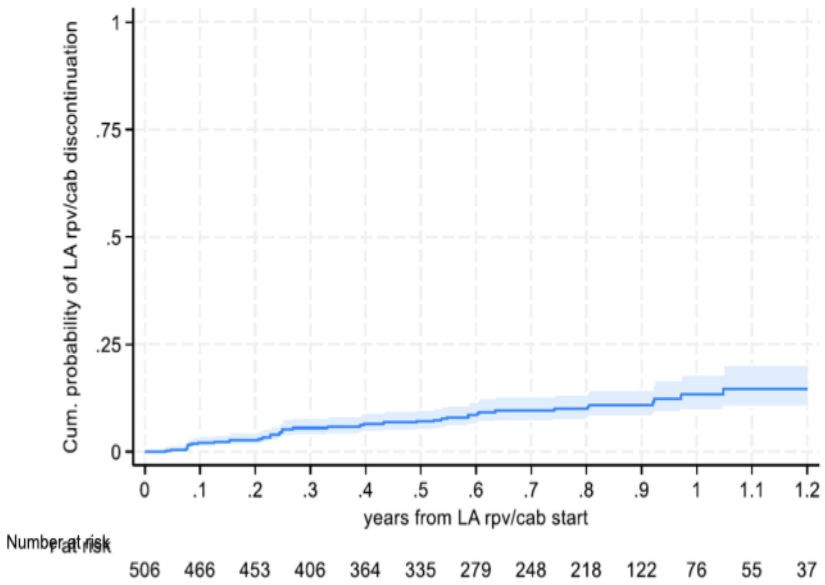
See next slides for foodnotes and abbreviations

ICONA

CAB+RPV LA: Low virologic failure rate in routine clinical practice

- **Study Design:** Observational cohort study
- **Objective:** Evaluate the effectiveness of CAB+RPV LA in the real-world, including risk of treatment discontinuation (TD), toxicity and virological failure
- 506 people with HIV initiated CAB+RPV LA, with a median follow-up of 8.7 months (IQR 4.8-10.8)
  - 11% female, 33% with >50 years, median 4 (IQR 3-5) previous lines of ART
  - 82% and 46% had a genotypic resistance test for RT and INI, respectively
- 47 (9.3%) individuals discontinued treatment for any cause, of which 51% switched to an oral 2DR
  - [redacted] cumulative probability of TD: 13.3% (95% CI: 9.7-18.1%); heterosexuals and PWID had higher risk
  - Injection site reactions were the most common cause of TD (n=17), followed by choice of PWH (n=11)
- 33 (6.5%) discontinuations occurred due to toxicity/AEs
  - 1-year cumulative probability of TD for toxicity/AEs: 10.1% (95% CI : 6.7-14.3%)
  - Heterosexuals had a higher risk of TD for toxicity/AEs, while females presented a lower risk
- 2 (0.4%) individuals experienced virological failure*
  - [redacted] cumulative probability of VF: 0.57% (95% CI : 0.14-2.38%)
  - 1 continued CAB+RPV LA and resuppressed, and 1 had NNRTI and INI RAMs at VF and was switched to BIC/FTC/TAF and then DRV/c/FTC/TAF and hasn't reached resuppression <50 c/mL

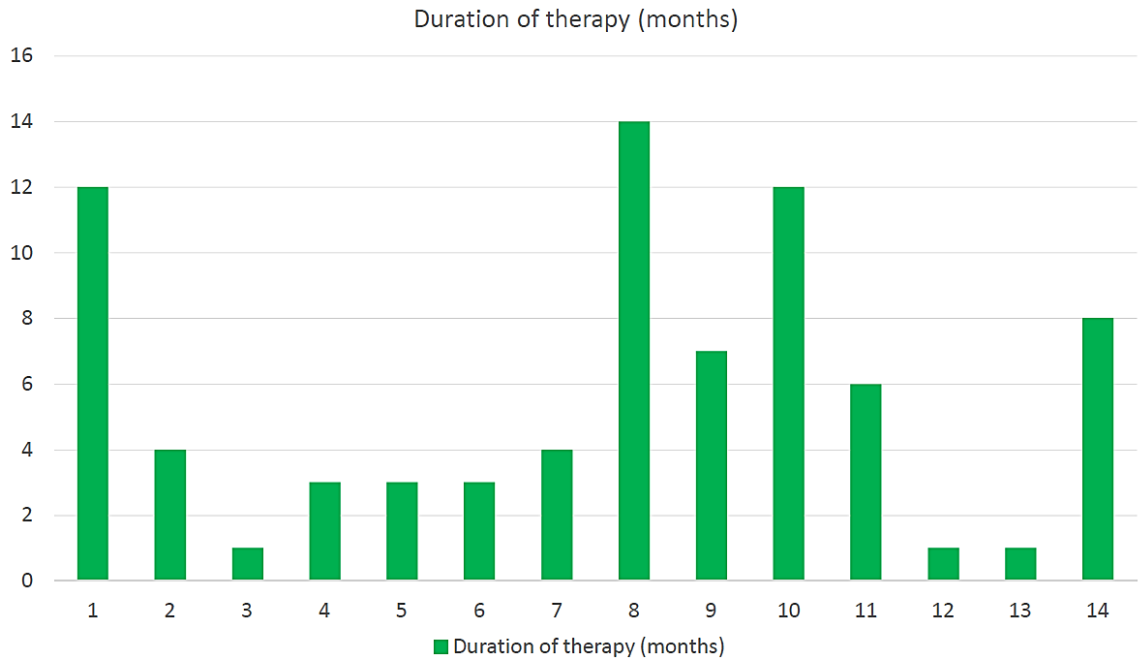
Probability of Treatment Discontinuation by Kaplan-Meier curve



SCOLTA

CAB + RPV LA Was Well Tolerated With a Low Rate of Virologic Failure in Italy

- **Study design:** A descriptive analysis of the causes of treatment interruption and the impact of genotypic drug resistance was conducted among people with HIV receiving CAB + RPV LA across 10 infectious disease units in Italy
- 758 individuals receiving CAB + RPV LA were included (average age, 53 years; average BMI, 25.26 kg/m^2)
- Average duration of LA therapy was 5.23 months
- 66 individuals (8.7%) interrupted treatment, with 14 (1.8%) interruptions due to VF
- 46 individuals had GRT before starting CAB + RPV LA, with 5 harboring NNRTI resistance and none harboring INSTI resistance
- Post-VF GRT revealed new mutations in 8 individuals
- Mean VL at failure was 2085 c/mL
- **Conclusions:** The rate of VF was consistent with other studies of CAB + RPV LA use. CAB + RPV LA was well tolerated. Selection of appropriate individuals for this regimen and awareness of risk factors for VF are crucial in reducing the risk of VF and the onset of new resistance mutations



GRT, genotypic resistance test.

. HIV Glasgow 2024; Glasgow, Scotland. Poster P074.

SCohoLART

Italian RWE supports the use of CAB+RPV LA

AIDS 2024

Italy

SCohoLART[1]

People living with HIV with long exposure to ART (N=504) Median follow-up: 9.4 months (6.4–11.4)

- Median age was 49 years
- Median of 14.4 years on ART

Key results

→ 48 participants (9.5%) discontinued CAB + RPV LA
  - Main cause was ISRs

→ 4 participants (0.8%) experienced VF*
  - 3/4 had NNRTI and INI RAMs at failure
  - All resuppressed on STRs

*CVF defined as VL ≥50 c/mL at 2 consecutive measurements or a single VL ≥1,000 c/mL for SCohoLART

1. Muccini C, et al. AIDS 2024. Poster THPEB104

GEPPO

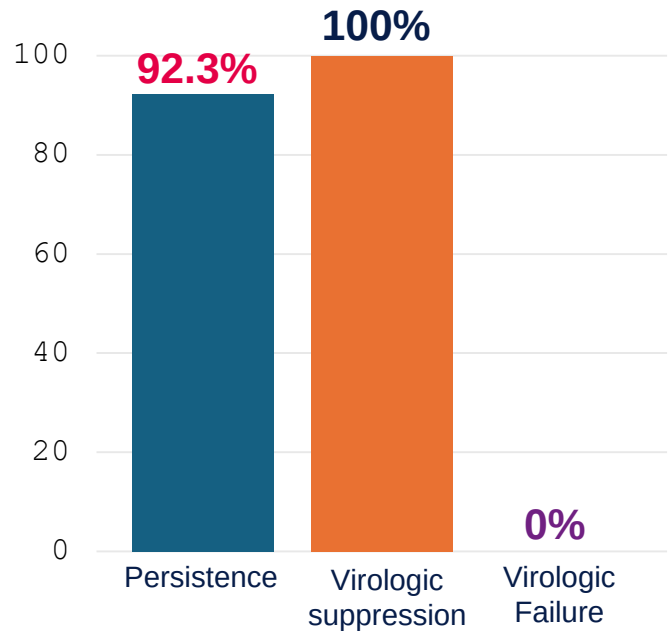
Use of CAB + RPV LA in individuals with VL ≥50 c/mL, with known or suspected resistance to, or prior virologic failure with agents of the NNRTI or INI class is outside of the labeled indication

CAB+RPV LA: High effectiveness and persistence among people with HIV aged ≥65 years

- **Objective:** Assess the effectiveness and safety of CAB+RPV LA in older people with HIV included in the GEPPO cohort
- 78 people with ≥65 years were included
  - Median age 66.7 years (IQR 65-70), 76% male at birth
  - Median 20 (IQR 14.0-28.5) years of HIV infection, and 19 (13-22) years on ART; 3 (3.8%) had VL >50 c/mL at initiation of CAB+RPV LA
  - 62% with multimorbidity (≥3 comorbidities), 32% with polypharmacy (≥5 medications other than ART)
  - 2 had history of NNRTI RAMs, 6 had A1/A6 subtype, 10 had BMI >30 kg/m^2
- After a median follow-up of 17.29 months (CI 95% 16.74-17.60), **72 (92.3%) participants were still receiving CAB+RPV LA, with 10 (12.8%) with >5 years follow-up**
  - 6 (7.7%) individuals discontinued CAB+RPV LA*
- **No virologic failures occurred and VL remained <50 c/mL in all people with HIV** and CD4+ cell count at last available observation was 656 (519-964) cells/mm^3
  - 3 individuals with VL >50 c/mL at initiation (55, 234, and 945 c/mL) were suppressed in the follow-up
  - 2 individuals with 2 potential risk factors for VF (subtype A6/A1 and BMI >30 kg/m^2) were on treatment and suppressed <50 c/mL at 1 and 13.1 months

Persistence and virologic outcomes, n=78

Median follow-up time: 17.29 months (CI 95%: 16.74-17.60)



No virologic failures and good tolerability profile among older people with HIV with a long ART history and high prevalence of multimorbidity and polypharmacy

Calcagno A, et al. CROI 2025; San Francisco, CA. Poster 677

*Reasons for discontinuation: palpitations and paresthesias; physician's choice (previous resistance to NNRTIs); hepatic flare in occult HBV; fever, myalgia and skin rash; death (unknown cause); and patient's choice

J Antimicrob Chemother
https://doi.org/10.1093/jac/dkaf025

Journal of Antimicrobial Chemotherapy 50 years

Question and answers on long-acting therapy with cabotegravir and rilpivirine in people with HIV

Lucia Taramasso [1]*, Stefano Bonora [2], Antonella Cingolani[3], Antonio Di Biagio [1,4], Nicola Gianotti [5], Giovanni Guaraldi [6], Sergio Lo Caputo[7], Giordano Madeddu [8], Paolo Maggi[9], Giulia Marchetti[10], Silvia Nozza [5,11], Stefano Rusconi[12] and Franco Maggiolo[13]

Table 1. Rates and characteristics of VF reported in observational cohort studies including people treated with LA cabotegravir and rilpivirine

Study	*n*	Median (IQR) follow-up, months	VF[a], % (*n*/*N*)	Time (range) to VF, months	BMI ≥30 kg/m^2[b]	Rilpivirine or cabotegravir RAMs at baseline[b]	Viral subtype A6[b]	RAMs at VF (*n*)
SCohoLART[54]	514	13.1 (9.1–15.5)	0.8 (4/514)	3–6	0/4	NR	0/4	3/4 NNRTI (K101PQ/E/KE, *n*=2; E138A/EA, *n*=3). 3/4 INSTI (E138K/EK, *n*=2; Q148R/Q148QR, *n*=2; E157Q, *n*=1).
SHARE LAI-net[55]	423	7.5 (3.7–11.3)	0.7 (3/423)	3–11	1/3	0/3	0/3	1/3 NNRTI (K101E)
Maguire *et al.*[56]	374	NR	0.8 (3/374)	1–8.4	2/3	0/3	0/3	1/3 NNRTI (K103E, I178M) 2/3 INSTI (Q148R, *n*=1; N155H, *n*=1; R263K, *n*=1)
OPERA[15]	321	4.2 (2.7–6.8)	1.2 (4/321)	1.4–8.4	NR	NR	NR	NR
Hill *et al.*[14]	287	15 (11.5–18.3)	1.0 (3/287)	NR	NR	NR	NR	NR
Swiss SHCS[57]	186	5.8 (0.5–43.8) in males and 3.7 (0.5–22.9) in females	1.6 (3/186)	5–15	1/3	NR	NR	0/3
Gutiérrez *et al.*[58]	173	11.1 (7.1–13.2)	1.1 (2/173)	1–3	2/2	NR	0/2	2/2 NNRTI (E138K, *n*=1; K181C, *n*=1) 1/2 INSTI (Q148QR,G263K)
Serris *et al.*[59]	126	9 (7–24)	4.0 (5/126)	1–32	1/5	0/2	0/5	0/2 NNRTI 0/3 INSTI
CUSTOMIZE[60]	102	12	0 (0/102)	—	—	—	—	—
WARD 86, people with suppressed viraemia[21]	76	7.7 (2.3–19.4)	0 (0/76)	—	—	—	—	—
Haser *et al.*[61,62]	74	NR	1.3 (1/74)	6	0/1	0/1	NR	1 NNRTI (K103N, L100I)
Adachi *et al.*[63]	74	13	0 (0/82)	—	—	—	—	—
Rubenstein *et al.*[64]	72	15 (11.7–16.8)	1.4 (1/72)	1	0/1	NR	NR	NR
JABS[65]	60	12	0 (0/60)	—	—	—	—	—
WARD 86, people with viraemia[48]	59	11.2	8.5 (5/59)	1–11.2	NR	NR	NR	5/5 NNRTI (E138K or E138A/K/T, *n*=3; L100I and Y181I or Y181C or Y181F/I/N, *n*=3; K101E, *n*=2; M230L, *n*=1) 2/5 INSTI (R263, K *n*=1; Q148R, *n*=1)
Konishi *et al.*[66]	38	10.3	0 (0/38)	—	—	—	—	—
Masich *et al.*[67]	24	Virological data were available for 14/24 participants at 3 months and for 7/24 at	4 (1/24)	1	1/1	0/1	0/1	0/1

Taramasso L et al. JAC 2

SLR: Emergent resistance after VF[1]

- **Inclusion criteria:** Real-world studies that identified VFs and reported RAM testing results at VF among people who were virologically suppressed at CAB+RPV LA initiation
  - 13 studies representing 2934 people with HIV in real-world cohorts were included
- **21 of 39 VFs had treatment-emergent resistance** reported across 11 studies
  - 18 (46%) had treatment-emergent NNRTI RAMs
  - **14 (36%) had treatment-emergent INSTI RAMs**
    - Most common major INSTI RAMs included Q148R (n=5), N155H (n=5), E138K (n=3), R263K (n=2), and G140S (n=2)
  - 10 (26%) had no genotype available at VF

RW
VF
RAM
HIV RNA <50 copies/Ml

Participants who experienced CVF in Phase III/IIIb trials resuppressed on oral ART

23/30 CVFs across Phase III/IIIb studies*
had treatment-emergent NNRTI and/or INSTI RAMs[1–8]

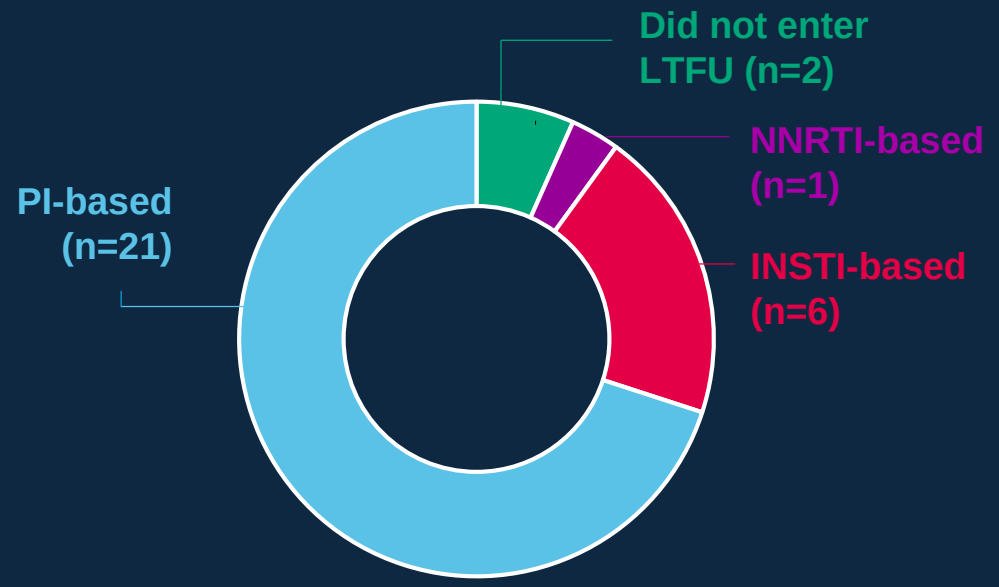
- 19 had treatment-emergent INSTI RAMs
- 21 had treatment-emergent NNRTI RAMs
- **<1% had treatment-emergent resistance with reduced phenotypic susceptibility to CAB or RPV**

93% of participants with CVF in Phase III/IIIb studies
resuppressed on alternative regimens†[9]

- The most commonly regimens used post-CVF were PI-based[9]

*Reported across ATLAS, FLAIR, ATLAS-2M, CARISEL, SOLAR and CARES; includes 1 non-protocol defined VF
†A total of 26/28 people with HIV resuppressed on alternative regimens (excludes one person with HIV who did not enter LTFU and one person with HIV who died of non-HIV causes before re-test
LTFU, long-term follow-up; **PI,** protease inhibitor

Post-CVF switch regimens in Phase III/IIIb studies†[9]



1. Ramgopal MN, et al. Lancet HIV 2023;10:e566-77 (and suppl. appendix)
2. Overton ET, et al. Lancet 2021;396:1994-2005 (and suppl. appendix)
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Participants who experienced VF in real-world studies resuppressed on oral ART

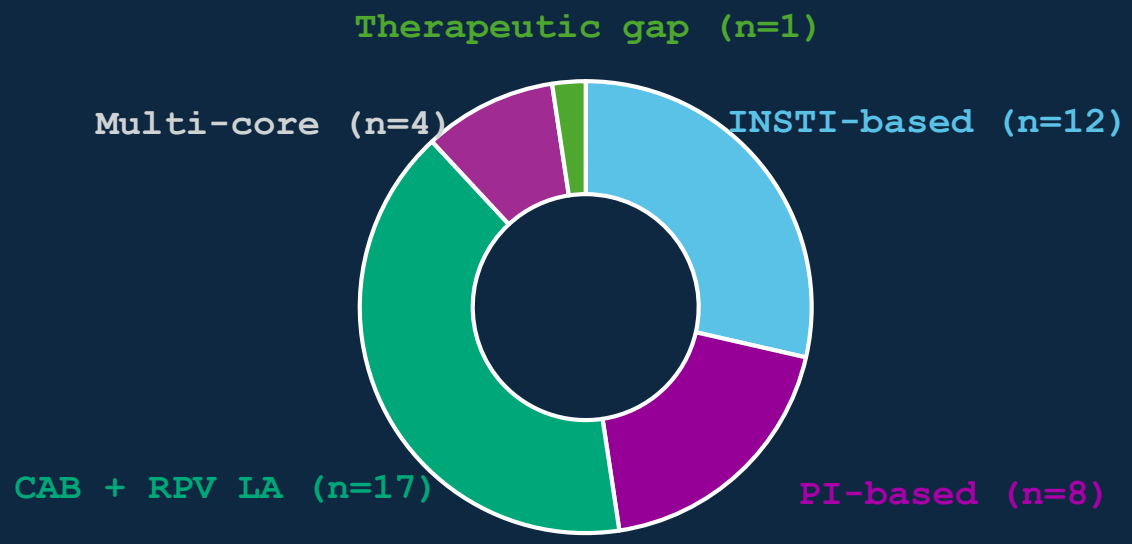
50 cases of VF were identified in a systemic literature review of real-world studies*

- Post-VF regimens were known in 42/50 cases of VF; outcomes were known in 32 cases with follow-up

85% of people with HIV with VF in real-word studies **resuppressed on alternative regimens**

- INSTI-based regimens were most frequently used post-VF

Post-VF switch regimens in real-world studies



*Systemic literature review used PubMed, Embase, Cochrane and 23 HIV-related conferences through March 2024 to identify all real-world cohorts evaluating CAB + RPV LA

Elias A, et al. HIV Glasgow 2024. Poster P062

E

MUTATIONS IN THE INTEGRASE GENE ASSOCIATED WITH RESISTANCE TO INTEGRASE STRAND TRANSFER INHIBITORS (InSTIs)[28]

	T 66	L 74	E 92	T 97	G 118	F 121	E 138	G 140	Y 143	S 147	Q 148	S 153	N 155	R 263
Bictegravir[29]					G 118 R		E 138 A K T	G 140 A C R S			Q 148 H K R	S 153 F Y		R **263** **K**
Cabotegravir[30]	T 66 K	L **74** **I***		T 97 A	G **118** **R**		E 138 A K T	G **140** A C **R** S			Q **148** **H** **K** **R**	S 153 F Y	N **155** **H**	R **263** **K**
Dolutegravir[29,31]					G **118** **R**		E 138 A K T	G **140** A C **R** S		S 147 G	Q **148** **H** **K** **R**	S 153 F Y	N 155 H	R **263** **K**
Elvitegravir[32]	T **66** **I** A K		E **92** **Q** G	T 97 A	G **118** **R**	F **121** **Y**	E 138 A K	G 140 A C S		S **147** **G**	Q **148** **H** **K** **R**		N **155** **H**	R **263** **K**
Raltegravir[33]		L 74 M	E 92 Q	T 97 A	G **118** **R**	F **121** **Y**	E 138 A K	G 140 A C S	Y **143** **R** **H** **C**		Q **148** **H** **K** **R**		N **155** **H**	R **263** **K**

*Relevant to subtype A6 only

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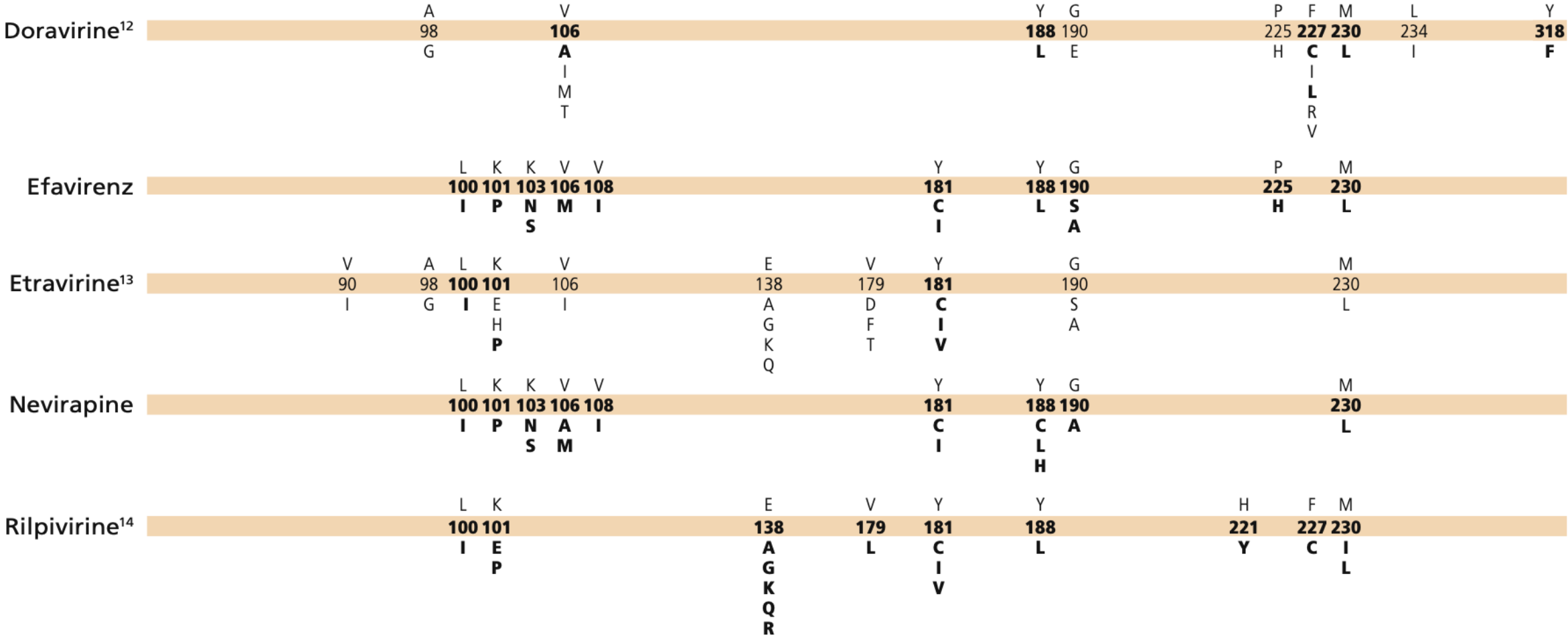
Nonnucleoside Analogue Reverse Transcriptase Inhibitors (NNRTIs)[1,11]



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A Proposal for a Tool to Reduce the Frequency of HIV RNA Monitoring in People with HIV Treated with Long-Acting Antiretrovirals

Gaia Cologgi,[1,2] Claudia Bartalucci,[1,2] Monica Melchio,[1,2] Lucia Taramasso,[2] Bianca Bruzzone,[3] Matteo Bassetti,[1,2] and Antonio Di Biagio[1,2]

THE GENOVA JOB

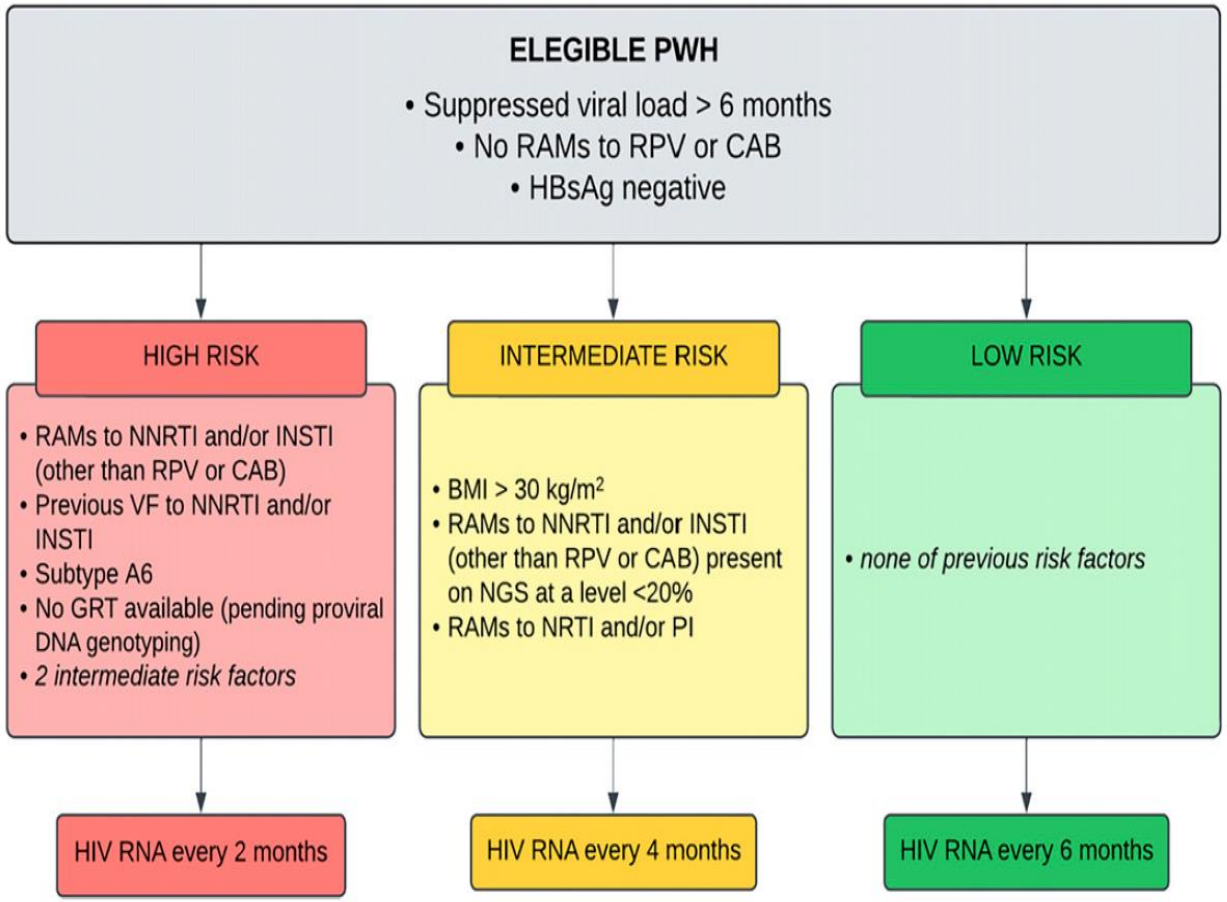
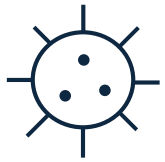


FIG. 1. Risk stratification of viral failure for PWH on long-acting RPV and CAB treatment. BMI, body mass index; CAB, cabotegravir; GRT, genotypic resistance test; HBsAg, hepatitis B surface antigen; INSTI, integrase strand transfer inhibitors; NGS, next-generation sequencing; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH, people with HIV; RAMs, resistance-associated mutations; RPV, rilpivirine; VF, virological failure.

CAB + RPV LA: People who experience VF maintain options for fully active oral regimens



The rate of VF with INSTI or dual-class resistance is low in clinical trials (0.7%)* and RWE†[1–9]

When VF with resistance does occur, people with HIV maintain future treatment options and most resuppress on oral ART[10]

- INSTI-based regimens were used for resuppression after VF in clinical trials and real-world studies, and many resuppressed while remaining on CAB + RPV LA

Patients should be counselled on the risk of VF with resistance; however, unique benefits including directly observed adherence, improved treatment satisfaction and preference versus daily oral therapy should be considered as part of shared decision making[11–15]

*Clinical trials: ATLAS, FLAIR, ATLAS-2M, CARISEL, SOLAR and CARES

†Across 13 real-world studies of 2,934 people with HIV receiving CAB + RPV LA, 39 VFs were reported and 14 VFs had INSTI RAMs at treatment failure. Results were obtained from a systematic literature review using PubMed, Embase, Cochrane and 23 HIV-related conferences through March 2024 to identify all real-world cohorts evaluating CAB + RPV LA. Data were extracted from studies that included individuals who were virally suppressed at initiation, identified VFs and reported on RAM testing results at VF. All studies that met these criteria were included regardless of treatment duration, follow-up period and VF definition used. Cohorts including <10 virally suppressed individuals were excluded

See next slide for references

Dobbiamo temere le resistenze ?

- **Stiamo affrontando una nuova fase di ART, differente dalle precedenti, ma non come la HAART**

- **Non bisogna avere timore, serve conoscere:**

Virus

Antiretrovirali

Uomo

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