Cabotegravir e rilpivirina: quali esperienze in persone con scarsa aderenza?

Dott.ssa Simona Di Giambenedetto

Università Cattolica del S. Cuore, Fondazione Policlinico Gemelli, IRCCS Roma

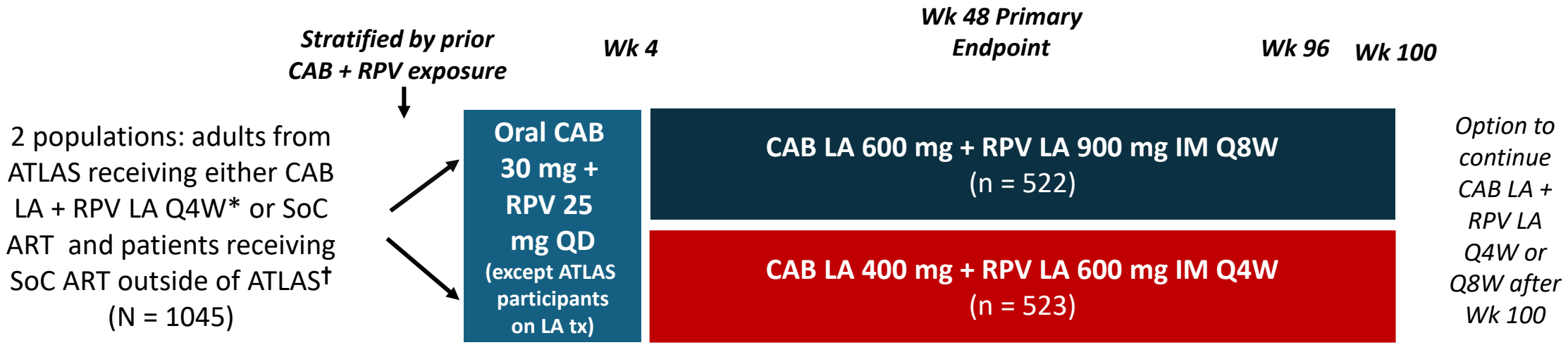
Disclosures

- **Grants for educational activities**
  - Merck Sharp and Dohme
  - ViiV Healthcare
  - Gilead

- **Personal fees for advisory boards and speakers bureau**
  - Merck Sharp and Dohme
  - ViiV Healthcare
  - Gilead

PRESENTE FUTURO: LA e ATLAS-2M Week 96 Results: Study Design

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



- Primary endpoint: HIV-1 RNA ≥ 50 copies/mL at W 48 by FDA snapshot in ITT-E
- Secondary/other endpoints: plasma HIV-1 RNA ≥ 50 or < 50 copies/mL at Wk 96 by FDA snapshot in ITT-E, safety and tolerability, VF in patients with CVF

Jaeger. CROI 2021. Abstr 401. NCT03299049.

SOLAR PHASE IIIB, RANDOMISED, OPEN-LABEL, MULTICENTRE TRIAL

- **670 participants**, virally supressed and taking BIC/FTC/TAF were randomised 2:1 to switch to CAB+RPV LA administered every two months (447 participants) or continue taking daily oral BIC/FTC/TAF (223 participants).

- At Month 12, **CAB+RPV LA demonstrated non-inferior efficacy versus daily oral BIC/FTC/TAF** based on the proportion of participants with HIV-1 RNA ≥50 c/mL

- At the beginning of the study, 47% of participants reported always or often experiencing one or more challenges with taking their daily therapy, including:

- ***"being worried about people unintentionally discovering their HIV status,"***
- ***"being worried about forgetting to take their HIV medication"***
- ***"feeling that taking their HIV medication was an uncomfortable reminder of their HIV status."***

- Mean **treatment satisfaction scores (HIVTSQs)** improved significantly at the conclusion of the study for participants taking CAB+RPV LA (+3.36) compared to BIC/FTC/TAF (-1.59) from baseline (CAB+RPV LA: 57.88, BIC/FTC/TAF: 58.38) ($p<0.001$).

90% of participants preferred long-acting therapy versus daily oral pills(n=382/425), with the **top five reasons for preferring long-acting therapy** being:

«I don't have to worry as much about remembering to take HIV medication every day»

«It is more convenient for me to receive injections every 2 months»

«I do not have to carry my HIV medication with me»

«I do not have to think about my HIV status every day»

«I do not have to worry about others seeing or finding my HIV pills»

GLI OSTACOLI DA CONSIDERARE

Punti di discussione

- Gradimento dei nostri pazienti per l'innovazione
- I nostri Ambulatori sono organizzati e il personale infermieristico è istruito?
- Strategie alternative per la somministrazione «fuori dagli Ambulatori Ospedalieri»

202 utenti intervistati:

Il principale beneficio indicato dai PLWH intervistati (68.8%) è la maggiore libertà grazie al non dover ricordare di assumere la terapia ogni giorno.

Il principale ostacolo indicato dai PLWH intervistati (51%) è il **fare l’iniezione in ospedale può essere un ostacolo.**

☑ All RECOMMENDATIONS: USE OF INJECTABLE CAB/RPV LA AS REPLACEMENT ART IN VIRALLY SUPPRESSED ADULTS

Patients for Whom CAB/RPV LA Is Not Recommended

- Before recommending a switch to CAB/RPV LA, clinicians should determine patients' hepatitis B status (hepatitis B surface antigen, core antibody, surface antibody, and HBV DNA if indicated); CAB/RPV LA should not be recommended for patients with active HBV coinfection [a] without concurrent oral therapy for HBV. (A*)
- Before recommending CAB/RPV LA for patients who have been treated previously with INSTIs or NNRTIs, clinicians should review results of prior resistance testing and ART treatment history or consider baseline genotypic resistance testing if no prior results are available; genotypic resistance testing should include both the reverse transcriptase and integrase genes. (A3)
- Clinicians should not recommend CAB/RPV LA in patients with known or suspected INSTI or NNRTI RAMs, excluding the K103N mutation in isolation, at baseline. (A1)
- Because there are no currently available data on the safety and efficacy of this regimen in children or adolescents or during pregnancy or breastfeeding, clinicians should not recommend treatment with CAB/RPV LA for these patients. (A*)
- Preexisting CAB and RPV RAMs have been associated with virologic failure; therefore, clinicians should obtain proviral DNA genotypic resistance testing before switching to CAB/RPV LA in any patient for whom historical resistance test results are not available. (B2)

Administration

- CAB/RPV LA should be administered by a licensed and trained healthcare professional. (A*)
- To prepare and administer CAB/RPV LA, clinicians should follow the protocols detailed in Box 2 and in the medication package inserts. (A1)

Dosing Strategy

- If an oral lead-in is chosen to assess medication tolerability, the clinician should prescribe up to 4 weeks of oral CAB/RPV. (A3)
- Once a dosing schedule is decided upon, clinicians should administer CAB/RPV LA as detailed in *Table 2: Optional Lead-in, Initiation, and Maintenance for Monthly CAB/RPV LA Dosing* or *Table 3: Optional Lead-in, Initiation, and Maintenance for Bimonthly CAB/RPV LA Dosing*; a bimonthly (every 8 weeks) dosing schedule is preferred. (A1)

Managing Missed Injections

- If a patient plans to miss or delay a monthly CAB/RPV LA injection by >7 days, the clinician should arrange for oral medication (CAB 30 mg and RPV 25 mg daily) to be available in advance in an adequate supply (up to 2 months/8 weeks) to cover the gap in injections.
- Clinicians should resume CAB/RPV LA in patients who miss injections as detailed in *Managing Missed or Delayed Injections*. (A3)

Utenti da semplificare in UCSC: 460 «20% della popolazione totale

DHHS/NYSDHAI guidelines. Use of Injectable CAB/RPV LA as Replacement ART in Virally Suppressed Adults. August

CLINICAL TRIAL vs REAL LIFE

TRIALS

- Paziente ideale
- Adeguata implementazione delle strutture dedicate
- Adeguata formazione del personale infermieristico dedicato
- Numerosità del personale adeguata a tutte le mansioni
- Aderenza del paziente alla somministrazione bimestrale del regime parenterale

REAL LIFE

- Pazienti fragili, comorbidi, anziani
- Non adeguamento sufficiente delle strutture dedicate
- Non sufficiente implementazione delle risorse dedicate
- Numerosità ridotta del personale dedito contemporaneamente ad altre numerose attività ambulatoriali
- Pazienti non sempre aderenti alla somministrazione bimestrale

Background

Review

The Promise of Improved Adherence With Long-Acting Antiretroviral Therapy: What Are the Data?

Kimberly K. Scarsi, PharmD, MS[1,2], and Susan Swindells, MBBS[2]

Trends in racial and ethnic disparities in antiretroviral therapy prescription and viral suppression in the United States, 2009–2013

Linda Beer, PhD[a], Heather Bradley, PhD[a], Christine L. Mattson, PhD[a], Christopher H. Johnson, MS[a], Brooke Hoots, PhD[a], and R. Luke Shouse, MD[a] for the Medical Monitoring Project

[a]Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA

Open Forum Infectious Diseases

MAJOR ARTICLE

Social Determinants of Health and Care Outcomes Among People With HIV in the United States

Timothy W. Menza,[1,2] Lindsay K. Hixson,[1] Lauren Lipira,[1,3] and Linda Drach[1]

[1]Public Health Division, Oregon Health Authority, Portland, Oregon, USA, [2]Division of Infectious Diseases, Department of Medicine, Oregon Health and Science University, Portland, Oregon, USA, and [3]School of Social Work, Regional Research Institute, Portland State University, Portland, Oregon, USA

The Association of Unmet Needs with Subsequent Retention in Care and HIV Suppression Among Hospitalized Patients with HIV Who Are Out of Care

Dima Dandachi, M.D.[1], Sarah B. May, M.S.[2,3], Jessica A. Davila, Ph.D.[2,3], Jeffrey Cully, Ph.D.[2,3,4], K. Rivet Amico, Ph.D.[5], Michael A. Kallen, Ph.D., M.P.H.[6], and Thomas P. Giordano, M.D., M.P.H.[1,2,3]

Clinical Infectious Diseases

MAJOR ARTICLE

First Demonstration Project of Long-Acting Injectable Antiretroviral Therapy for Persons With and Without Detectable Human Immunodeficiency Virus (HIV) Viremia in an Urban HIV Clinic

Katerina A. Christopoulos,[1] Janet Grochowski,[1] Francis Mayorga-Munoz,[1] Matthew D. Hickey,[1] Elizabeth Imbert,[1] John D. Szumowski,[1] Samantha Dilworth,[2] Jon Oskarsson,[1] Mary Shiels,[1] Diane Havlir,[1] and Monica Gandhi[1]

«Of **24 patients** who initiated CAB/RPV-LA with viral suppression (median CD4 cell count, 706 cells/mm3), 19 (79%) DTI with a median of 6 injections (range, 2–8), 100% (95% CI, 86%–100%) **maintained viral suppression after starting injections**.»

«Of 15 patients who started with detectable viremia, (median CD4 cell count, 99 cells/mm3; mean log10 viral load, 4.67 with standard deviation 1.16), **all DTI with a median of 6 injections (range 3–11,), 12 (80%; 95% CI, 55%–93%) had achieved and maintained viral suppression, including the patient with the baseline N155H mutation.** For the 3 patients who had not yet achieved viral suppression, all had

Clinical Infectious Diseases

MAJOR ARTICLE

48-week viral suppression rates in people with HIV starting long-acting CAB/RPV with initial viremia

Matthew D Hickey[1], Nathanael Gistand[1], Janet Grochowski[1], Francis Mayorga-Munoz[1], Elizabeth Imbert[1], John D. Szumowski[2], Jon Oskarsson[1], Mary Shiels[1], Samantha Dilworth[1], Ayesha Appa[1], Diane V Havlir[1], Monica Gandhi[1], Katerina Christopoulos[1]

«**Five had VF with resistance (three with RPV-associated mutations,** two with CAB and RPV-associated mutations) and one was lost-to-follow-up. At week 48, two of those with VF were suppressed on alternative regimens (lenacapavir+BIC/TAF/FTC and CAB+lenacapavir). **Overall week 48 VS on either LA-CAB/RPV or alternative ART was 92% (54/59)**»

«Long-acting ART can be an important tool for improving VS among patients who face adherence challenges to oral ART»

JOURNAL ARTICLE CORRECTED PROOF

Comparison of At-Home Versus In-Clinic Receipt of Long-Acting Injectable Cabotegravir/Rilpivirine

MEDICAL UNIVERSITY OF SOUTH CAROLINA

Clinical Infectious Diseases

Get access >

Stephanie E Kirk ✉, Christina Young, Hayley Berry, Rochelle Hanson, Angela Moreland, Virginia Fonner, Mulugeta Gebregziabher, Jamila Williams, Eric G Meissner ✉

- 12-month intervention (from August 2021 to December 2022) for person receiving CAB+RPV under direction of their primary HIV provider every 2 months. First injection was always given in clinic.
- Subsequent injections research **participant decide to receive in clinic or at-home**, crossover allowed any time.
- For at home injections, participant received a stored medication in their own refrigerators prior to an LPN visit or administration (they also could opt to have an ephinephrine pen available).

The **33 enrolled participants**. Three stopped LA CAB/RPV and transitioned to oral antiretroviral therapy due to allergy (1), loss of virologic suppression (1), and visit adherence (1) concerns.

A comparable number of participants received treatment primarily in clinic (n = 18) relative to at home (n = 15).
Injection site pain/soreness was common (52% of injections) but did not differ between groups. There were no differences in safety or efficacy between groups and both groups reported high treatment satisfaction. **All participants were virologically suppressed and retained in care at the end of the study.**
At-home administration of LA CAB/RPV by a healthcare provider was comparably safe, effective, and associated with high participant satisfaction relative to in-clinic administration.

Real-Life Experience of Long-Acting Cabotegravir–Rilpivirine Combination in a Person Living with HIV with Detectable Viremia: A Case Report

Arturo Ciccullo,[1] Valentina Iannone,[2] Francesca Lombardi,[3] Alberto Borghetti,[3] and Simona Di Giambenedetto[2,3]

- *….A decision was made, given the lack of adherence to daily treatment, to start parenteral therapy with CAB+RPV. She was hence switched to 1 month of oral CAB+RPV and was then prescribed injectable CAB+RPV administered every 4 weeks, with first administration on* ***October 19, 2022.***
- *The new parenteral treatment was well tolerated, with no reported adverse events. After 4 weeks, HIV-RNA was 58 copies/mL and CD4+ cell count 327 cell/mm3. After 12 weeks, HIV-RNA was below 50 copies/mL and CD4+ cell count was 406 cell/mm3…*

HOME CARE ASSISTANCE: UTD

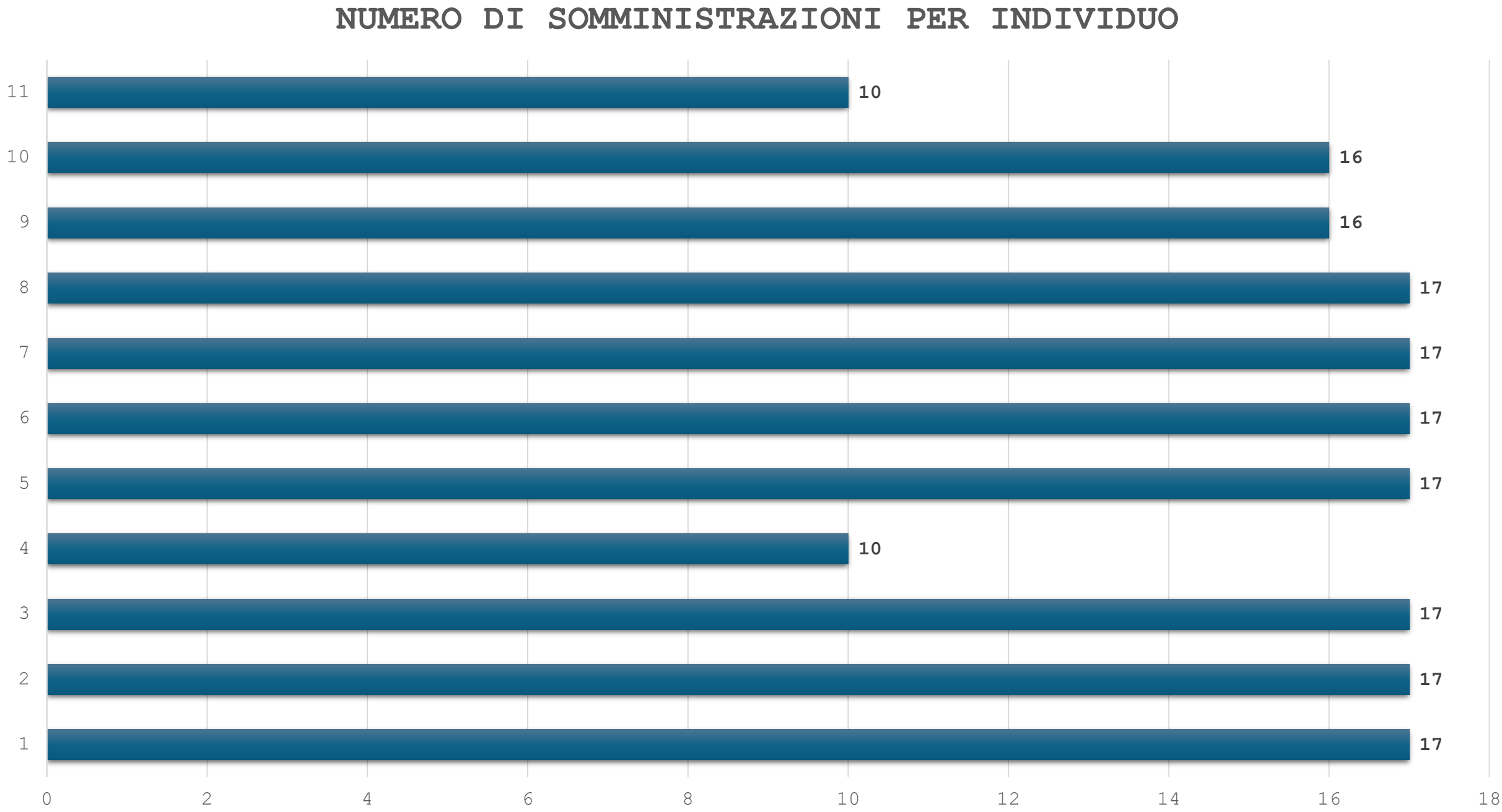
- Da ottobre del 2022 abbiamo iniziato somministrazione domiciliare a pazienti fragili, anziani e comorbidi;
- Personale infermieristico del servizio già presente e attivo (2), formato e specializzato;
- Possibilità di schedulare somministrazioni tramite il **calendario del servizio UTD** già presente e gestito da personale infermieristico dedicato;

- Utilizzo di una rete di servizio medico e infermieristico al domicilio del paziente fragile già presente e avviata
- Possibilità di eseguire una DOT therapy per individui non aderenti ai regimi oral e comorbidi.

Variabili	UTD N=11	P value
Age, median, years, (IQR, range)	55 (50-61)	0.040
Male sex, n (%)	6 (54.5)	0.240
Years of HIV infection, median (IQR)	15.7 (5.1-30.3)	0.543
Years of ART exposure, median (IQR)	15 (4-26)	0.382
CDC Stage C, n (%)	7 (63.6)	0.004
Zenith HIV-RNA as log10 copies/mL, median (IQR)	5.17 (4.68-5.80)	0.342
Nadir CD4+ cell count, median (IQR)	47 (25-269)	0.025
Oral lead in, n (%)	1	
BMI, Kg/m2, median (IQR)	22.65	
TCD4+ cells/mm3, median (IQR) at BL	476 (239-740)	0.031
CD4/CD8 ratio cells/mm3, median (IQR) at BL	0.50 (0.40-1.53)	0.057
HIV-RNA at BL > 30 cp/ml (switch to LA CAB+RPV)	1 (9.1%)	
Antiretroviral regimen before BL, n (%) - 2NRTI+INI - 2NRTI+NN - 2NRTI+PI - 3TC-based 2DR - Other	8 (72.7) 0 0 2 (18.2) 1 (9.1)	0.025

COMORBIDITIES

Comorbidità	UTD n=11	p
Cardiovascolari	5 (45.5)	0.044
Endocrinological disorders (DMTII, obesity)	3 (27.3)	0.313
Cancro	1 (9.1)	0.467
Psichiatriche	5 (45.5)	0.003
Epatologiche	2 (18.2)	0.360
Neurologiche	6 (54.5)	<0.001
Polmonari (BPCO)	1 (9.1)	0.284


NUMERO DI SOMMINISTRAZIONI PER INDIVIDUO
11
10
9
8
7
6
5
4
3
2
1
10
16
16
17
17
17
17
10
17
17
17
0
2
4
6
8
10
12
14
16
18

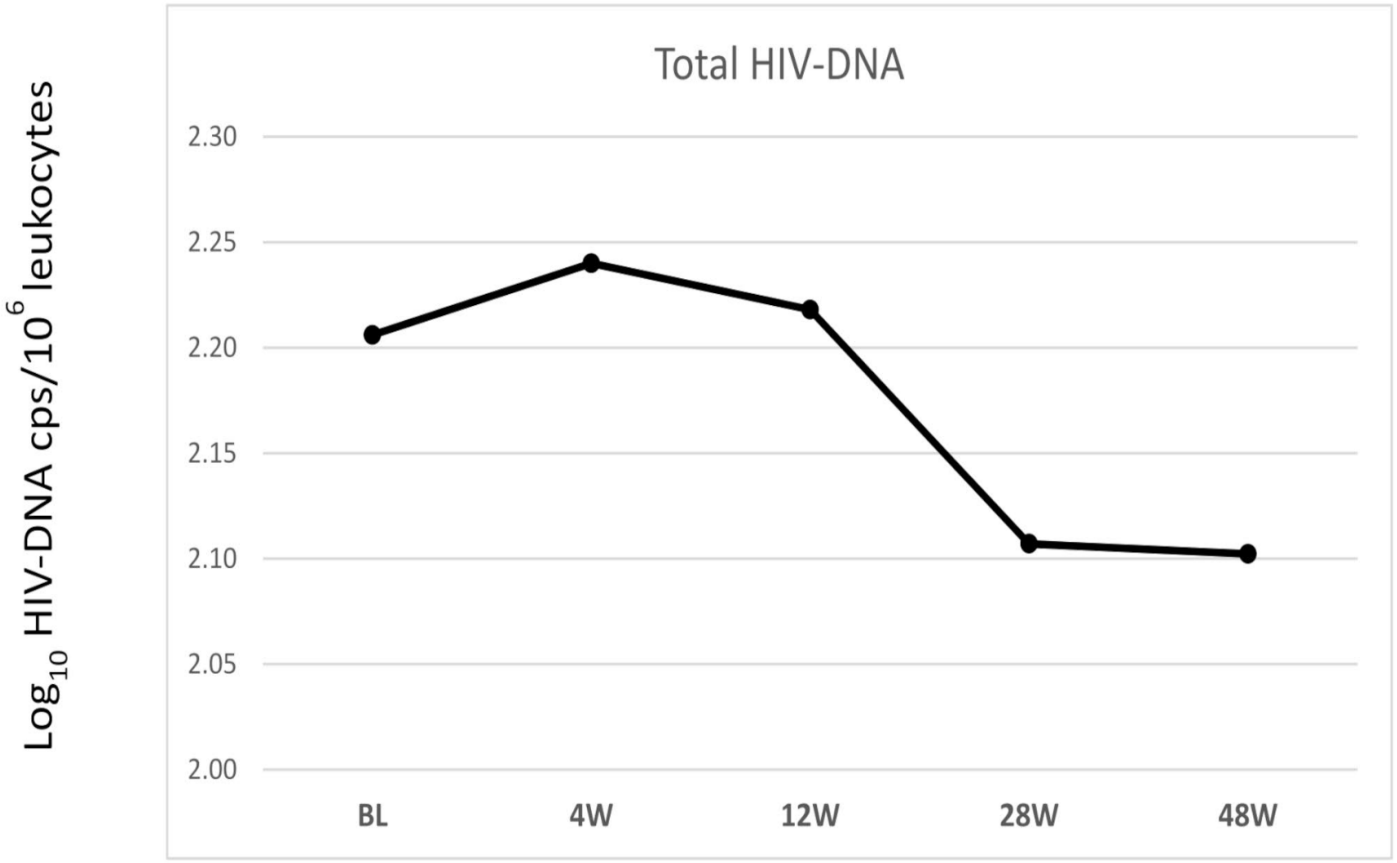
FOLLOW-UP and DISCONTINUATION

- During a 31.5 person-years follow-up (PYFU), all participants maintained virological suppression (< 30cps/mL).
- Regarding the immunological parameters, the analysis showed a non-significant change in absolute CD4+cell count at week 24 (p=0.503) and week 48 (p = 0.141);
- Meanwhile, we registered a significant improvement in CD4/CD8 ratio (median+0.13, p=0.005) at 48 weeks of follow-up.

- **The participant with detectable viremia at BL (86 cps/mL) achieved viral suppression at 24 W.**
- Only one virological failure was observed (HIV RNA 120 cp/ml, no resistance associated mutation detected on HIV DNA).

- We registered only 3 discontinuation to CAB+RPV due to:

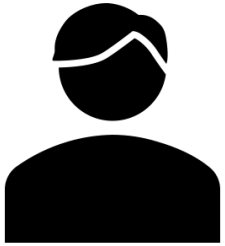
- **DDI (methadone d-d interaction), (9.1%)**
- **Pregnancy desire (PMA) (9.1%)**
- **Virological failure (9.1%)**



- Regarding the HIV-DNA analysis in this subgroup, the GLM-ANOVA revealed **no significant main effect of time (after each injection) on the HIV-DNA levels (p = 0.332).**
- However, the BL HIV-DNA level was 2.21 (95% CI 1.87–2.53); in fact, **a slight increase was observed after the first dose (2.24, 95% CI 1.98–2.50) followed by a downward trend from the second dose, 4w,** (2.11, 95% CI 1.68–2.53) up to 28 W, which, **however, was not statistically significant** (p = 0.900); finally, a **trend towards steadiness** was observed up to 48 W (2.10, 95% CI 1.76–2.44).

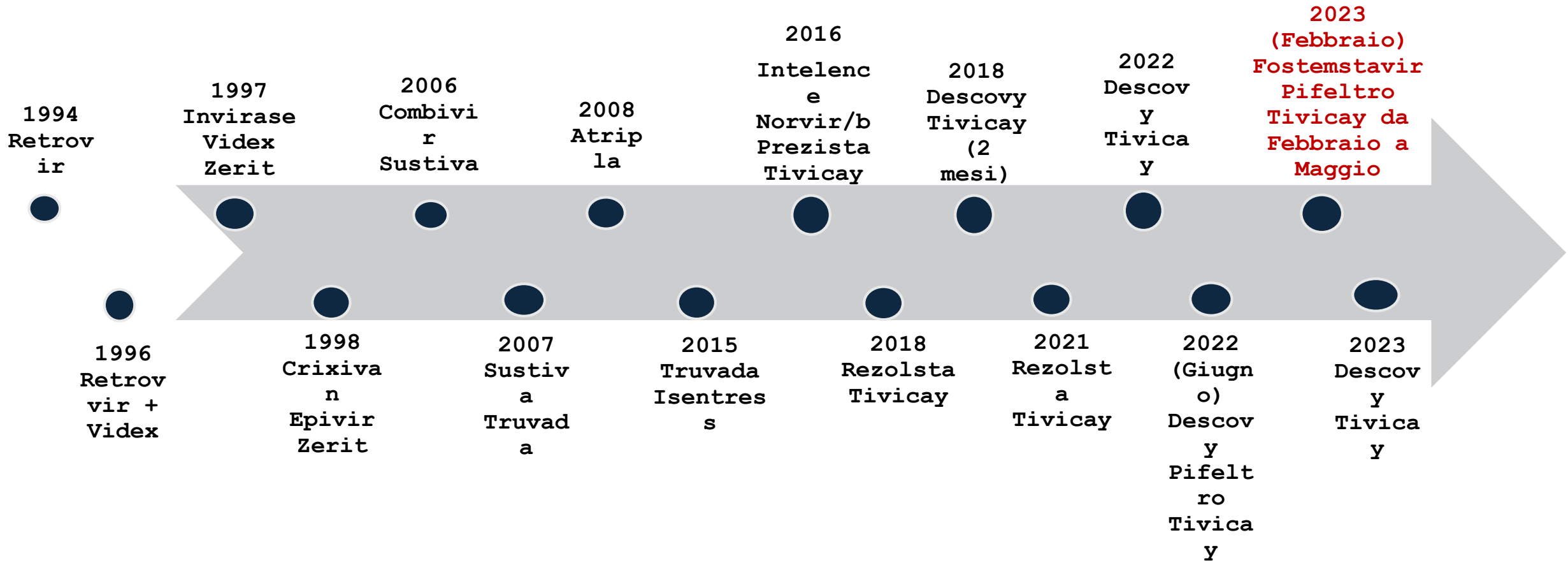
CASO CLINICO

55 aa

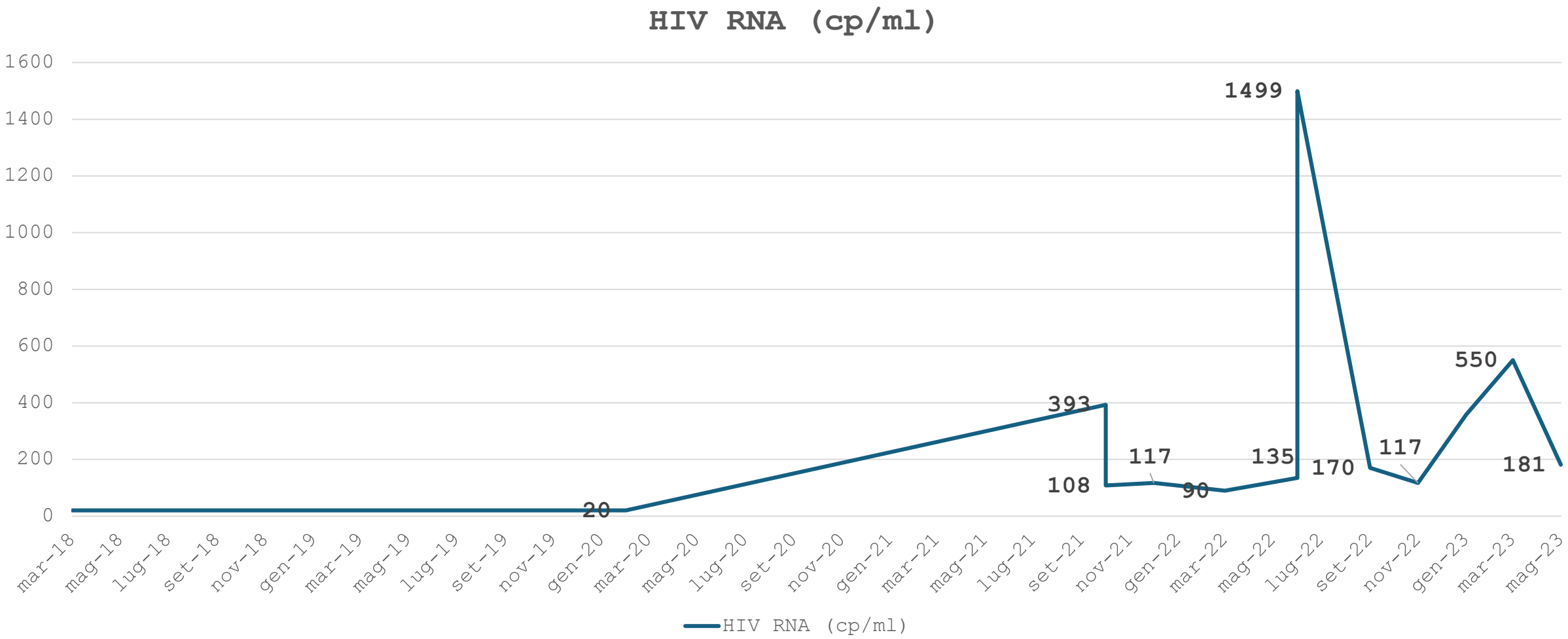


- Storia di **abuso di sostanze stupefacenti:** Cannabis, Cocaina, Eroina
- Fumo di sigaretta circa 8 anni (15 sigarette/die)
- Padre deceduto per carcinoma polmonare all'età di 74 anni/ madre di 84 anni portatrice di PMK.
- **Diagnosi di infezione da HIV** nel 1994 CDC B3 (**Zenith 105.000 cp/ml, Nadir TCD4+ 41 cell/mmc**).
- **Infezione da HCV dal 1994,** trattata con terapia antivirale nel 1996.
- Sierologia per HBV come da infezione pregressa (Anti HBcAg pos, HBV DNA neg)
- **Linfoma di Hodgkin stadio IV B** con localizzazioni linfonodali sovra e sottodiaframmatiche polmonari epatiche e spleniche, scheletriche e osteomidollari (diagnosticato nel 2021 in corso di ricovero su biopsia di linfonodo addominale), sottoposto a 6 cicli di terapia secondo ABVD con risposte DS 2 all'interim PET
- **Lipodistrofia nel 1999**

Regimi di terapia antiretrovirale



HIV RNA 2018-2023

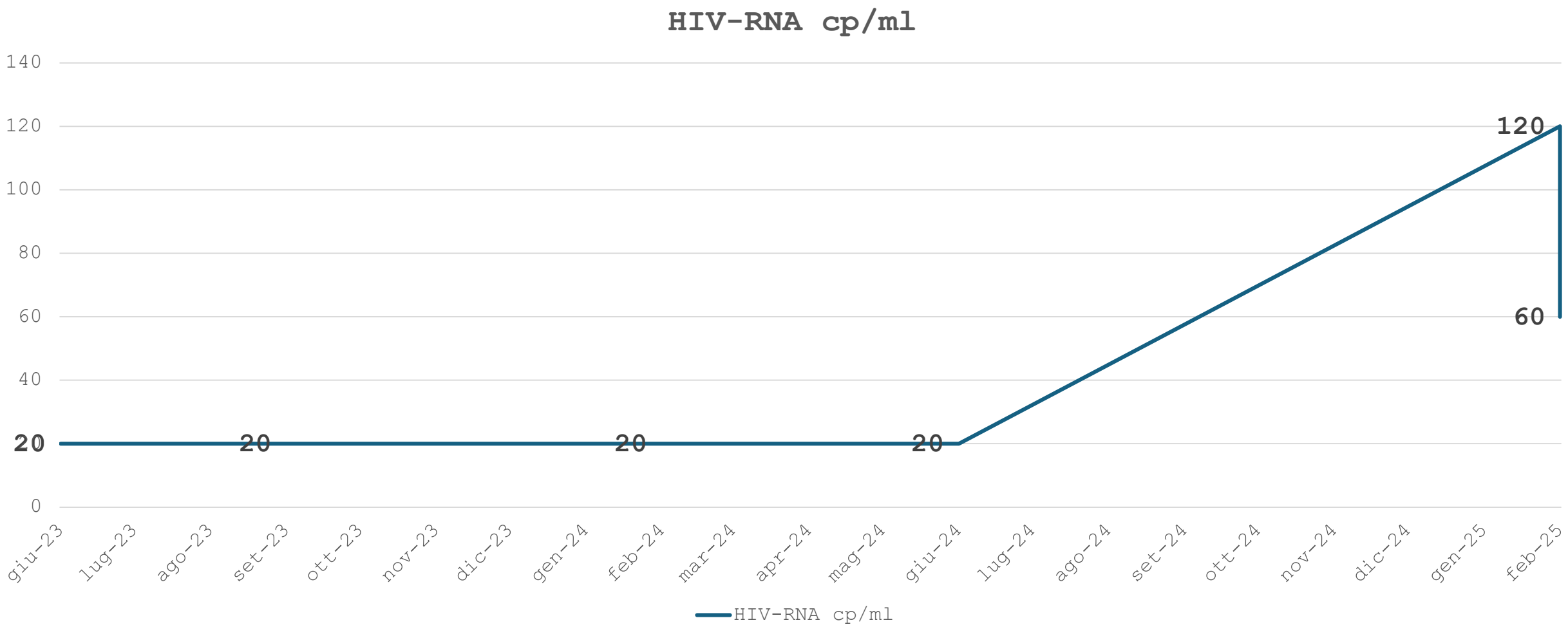


Home care Assistance-LA

Novembre 2023

SWITCH DI TERAPIA A LA CAB+RPV DOPO ADEGUATO COUNSELLING CON IL PAZIENTE CHE ACCETTA

HIV RNA in corso di LA CAB+RPV



TEST ESEGUITO SU DNA LINFOMONOCITARIO

MUTAZIONI NOTE:

PROTEASI: L63P (99%), V77I (100%), I93L (95%)

TRASCRITTASI INVERSA: D67N (96%), K70G (99%), M184V (99%), T215Y (99%)

INTEGRASI: NESSUNA

ALTRE MUTAZIONI:

PROTEASI: K14R, I15V, N37D, I62V

TRASCRITTASI INVERSA: K20R, V118I, D123E, I135T, T139S, Q174N, R211K, F214L

IN. S17N, A23V, S24G, L28I, S119P, T122I, V165I, V201I, K219N, N222K, D256E

RISULTATO:

PR: Presenza di mutazioni secondarie
RT: Presenza di mutazioni conferenti resistenza di vario grado agli NRTI
IN: Assenza di mutazioni conferenti resistenza agli inibitori dell'Integrasi

FARMACI POTENZIALMENTE EFFICACI:

PR: Tutti
RT: v. interpretazione
IN: Tutti

NOTE: L'analisi filogenetica della sequenza nucleotidica ha identificato un sottotipo B di HIV-1
Test eseguito con metodica ultrasensibile di sequenziamento (NGS) ed analizzato per il riconoscimento delle specie minoritarie con un cut off ≥ 5%.

INTERPRETAZIONE VIROLOGICA: Il presente quadro genotipico, ottenuto su DNA linfomonocitario (Vl= 121 cp/ml), evidenzia un fallimento virologico a basso numero di copie senza emergenza di nuova resistenza alla terapia attualmente in corso. Tale genotipo risulta sovrapponibile a quello di gennaio 2023, sempre su DNA in cui si conferma in **Trascrittasi Inversa** la presenza delle mutazioni associate a resistenza ad AZT, 3TC, FTC, Abacavir, tenofovir (parziale). Assenza di mutazioni di resistenza agli NNRTI ed INSTI anche in forma minoritaria.

- **Genotipo di resistenza su DNA Febbraio '25**

↓

SWITCH DI TERAPIA ANTIRETROVIRALE A TAF/FTC/DRV/c

LIMITATIONS IN OUTPATIENT SETTING

- Struttura ambulatoriale ancora inadatta ad accogliere un incremento di numero considerevole della coorte, per assenza di stanze dedicate
- Personale infermieristico non numericamente adeguato e dedito anche alle attività ordinarie quotidiane ambulatorio/DH
- Difficoltà nei reminder dei «missed appointments» e della gestione dell'agenda e dei contatti telefonici (assenza di personale dedicato)

…Long acting CAB+RPV come terapia innovativa per PWH ambulatoriali o come possibilità di superare i limiti all'aderenza e raggiungere le popolazioni più fragili?...

PROGRESS-HIV/MST

(Percorsi Rinnovati ed Ottimizzati per la Gestione e la Riorganizzazione in base alle Esigenze dei pazienti e dei Servizi Sanitari per problematiche complesse di persone che vivono con HIV o a rischio di MST)

Champion: Dott.ssa S. Di Giambenedetto

Coordinator: Prof. C. Torti

Attivazione di un **percorso** clinico-assistenziale, approvato dalla Direzione Sanitaria della Fondazione Policlinico Universitario A. Gemelli IRCCS e dal Dipartimento di Scienze Mediche e Chirurgiche in data **17/03/25** con i seguenti obiettivi:

- Realizzazione di un modello organizzativo dedicato all'assistenza di persone con HIV eleggibili alla somministrazione di **terapia long-acting** e **farmaci innovativi;**
- Facilitazione dell'accesso appropriato e consapevole a strategie diagnostiche e preventive per HIV (**PrEP**) e malattie sessualmente trasmissibili (**MST);**
- Sviluppo di strumenti digitali basati sull'implementazione della piattaforma **Patient Portal** per il monitoraggio continuativo (salute, qualità percepita, PROMs);
- Promozione della **vaccinazione** per la salvaguardia della salute sessuale;
- Attivazione dello **Sportello PROGRESS.**

Sponsorizzazione non condizionante di ViiV e Gilead

Ambulatorio 3 → PrEP, diagnosi e terapia di MST, gestione terapie LA

Ambulatorio 5
Ambulatorio 6
Ambulatorio 7
→ Gestione clinico-assistenziale esclusivamente dedicata a persone con infezione da HIV

- Personale infermieristico dedicato;
- Care manager: figura dedicata alla gestione delle agende, reminder degli appuntamenti, coordinamento degli accessi a prestazioni specialistiche;
- Sportello PROGRESS: punto unico di accesso dedicato all'orientamento dei pazienti nei percorsi HIV, PrEP e MST

1 Aprile 2025

- **67** persone con infezione da HIV in terapia intramuscolare long-acting;
- **3** slot al giorno dedicati alla somministrazione.

28 Aprile 2025

- **80** persone con infezione da HIV in terapia intramuscolare long-acting + **12** in fase di valutazione (in attesa del GRT su DNA o con prima somministrazione da pianificare);

GRAZIE PER L'ATTENZIONE