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ViiV Healthcare

VOCABRIA▼ cabotegravir sospensione per iniezione + REKAMBYS▼ rilpivirina sospensione per iniezione

VOCABRIA iniettabile è **indicato**, in associazione con rilpivirina iniettabile, per il trattamento dell'infezione da virus dell'immunodeficienza umana di tipo 1 (HIV-1) negli adulti in soppressione virologica (HIV-1 RNA <50 copie/mL) con un regime antiretrovirale stabile, senza evidenza presente o passata di resistenza virale e di precedente fallimento virologico agli agenti della classe degli NNRTI e degli INI.[2] **Classe di rimborsabilità:** H. **Prezzo al pubblico:** € 1795,70.** **Regime di dispensazione:** medicinale soggetto a prescrizione limitativa, da rinnovare volta per volta, vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti-infettivologo (RNRL).
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VOCABRIA compresse è **indicato**, in associazione con rilpivirina compresse, per il trattamento a breve termine dell'infezione da virus dell'immunodeficienza umana di tipo 1 (HIV-1) negli adulti in soppressione virologica (HIV-1 RNA <50 copie/mL) con un regime antiretrovirale stabile, senza evidenza presente o passata di resistenza virale e di precedente fallimento virologico agli agenti della classe degli NNRTI e degli INI per:
- la fase di induzione orale, atta a determinare la tollerabilità di Vocabria e rilpivirina prima della somministrazione della formulazione iniettabile, a lunga durata d'azione, di cabotegravir e rilpivirina
- la terapia orale per coloro che non possono presentarsi alla visita pianificata per l'iniezione di cabotegravir e rilpivirina.[2] **Classe di rimborsabilità:** H. **Prezzo al pubblico:** € 900,79.** **Regime di dispensazione:** medicinale soggetto a prescrizione limitativa, da rinnovare volta per volta, vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti-infettivologo (RNRL).
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Esperienze dalla real life: patologia cardiovascolare e uso di long acting nelle persone che vivono con HIV.

Experiences from real life: cardiovascular disease and long-acting use in Persons Living with HIV.

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La patologia cardiovascolare rappresenta tuttora la principale comorbilità nelle Persone che Vivono con HIV (PLWH): una mole notevole di dati accumulati negli anni ha infatti evidenziato che i nostri pazienti presentano un rischio di infarto del miocardio doppio rispetto alla popolazione generale, e il dato è stato confermato da un recente studio della Swiss Cohort (1). Appare dunque interessante in quest'ottica il lavoro monocentrico senese pubblicato in questo numero da Gasparro e colleghi (2) che indaga sulla prevalenza dei fattori di rischio cardiovascolare e sui predittori di ipertensione arteriosa, dislipidemia e diabete mellito tipo II nei PLWH. All'analisi multivariata la dislipidemia è risultata associata ad ipertensione arteriosa, precedente esposizione a inibitori della proteasi (PIs), HIV-RNA rilevabile ed età maggiore di 50 anni. L' ipertensione arteriosa è risultata associata a dislipidemia, età maggiore di 50 anni e BMI superiore a 30 kg/m^2. Il diabete mellito di tipo II infine è risultato associato all'ipertensione arteriosa. È interessare osservare come, nell'esperienza dei colleghi, i fattori di rischio tradizionali si combinino con fattori legati alla patologia, come la viremia rilevabile, e con la precedente esposizione ad una classe di farmaci antiretrovirali e come, da questa interazione, sia evidente il ruolo dell'infezione come fattore di rischio indipendente per malattia cardiovascolare.

Gi studi in *real life* restano sempre uno strumento prezioso per integrare le osservazioni dei più blasonati trials clinici randomizzati in termini di efficacia, sicurezza e tollerabilità. In quest'ottica Laura Labate e i colleghi di Genova (3) hanno condotto una osservazione sulla terapia in *single tablet regimen* al momento più utilizzata: quella con bictegravir associato a emtricitabina e a tenofovir alafenamide. Anche in questo caso lo studio è monocentrico, ma si avvantaggia di un numero non trascurabile di PLWH valutati (475 tra *experienced* e *naives*). L'osservazione a 24 mesi ha mostrato che il 90% dei PWH ha progressivamente raggiunto una viremia non rilevabile, che nell'11.7% dei casi si era registrata una discontinuazione del trattamento, ma solo in un caso si era avuto fallimento virologico e che, infine, l'incremento delle cellule CD4+ nei pazienti *naives* era stato considerevole, passando da una media di 353.8 a 612.8/µl.

Il numero comprende anche un report a firma di Andrea De Vito e Giordano Madeddu (4) dal recentissimo EACS 2023 tenuto a Varsavia, che ha selezionato gli studi presentati con argomento malattia cardiovascolare e trattamenti long-acting. Tra gli studi selezionati dal report ve n'è uno che mostra come il cambio a dolutegravir non aumenti il rischio cardiovascolare rispetto ai PIs. Questo è un dato utile, alla luce dell'acceso dibattito suscitato dai risultati dello studio RESPOND, che suggeriscono invece l'ipotesi di un rischio aumentato di infarto del miocardio in PLWH in trattamento recente con inibitori delle integrasi (5). Un altro studio illustrato dal report (6) mostra come i nuovi modelli di valutazione del rischio cardiovascolare, applicati alla Swiss Cohort, sembrino presentare maggiore accuratezza rispetto ai modelli più vecchi. Altri studi illustrano come interventi mirati hanno portato a miglioramenti

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cognitivi, e come la fragilità nelle persone anziane progredisca rapidamente nei PLWH. Il report illustra anche come l'esperienza del trattamento con cabotegravir e rilpivirina *long acting* ha dimostrato alta efficacia e tollerabilità, con bassi tassi di fallimento virologico, ma ricorda anche che la gestione degli effetti collaterali e le rare reazioni allergiche richiedono un attento monitoraggio e supporto, soprattutto nelle fasi iniziali della terapia.

Questo numero del giornale è completato da un interessante *case report* di un PLWH con comorbilità rappresentata da carcinoma avanzato del colon retto, che è stata con tutta probabilità causa di una meningite da E coli. Va sottolineato il crescente ruolo delle neoplasie non HIV-correlate che, combinandosi con la possibile condizione di immunodeficit può portare a quadri complessi come questo. ■

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Fattori di rischio cardiovascolare negli individui che vivono con HIV: uno studio osservazionale retrospettivo monocentrico.

Cardiovascular risk factors in People Living With HIV: a single centre retrospective observational study.

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Riassunto

Le patologie non-AIDS-definenti sono una sfida emergente, in particolare le patologie cardiovascolari, grazie all'incremento dell'aspettativa di vita degli individui che vivono con HIV (PLWH). Scopo del lavoro è descrivere la prevalenza dei fattori di rischio cardiovascolare e investigare i predittori di ipertensione arteriosa, dislipidemia e diabete mellito tipo II nei PLWH. È stato condotto uno studio retrospettivo cross-sectional analizzando i dati dei PLWH seguiti presso l'UOC di Malattie Infettive dell'Azienda Ospedaliera Universitaria Senese nel 2020-2021.

Sono stati arruolati 286 PLWH: 70% maschi, età mediana 54,4 interquartile range (IQR) 46,8-59,5, 33% fumatori, con un tempo mediano dalla diagnosi di 14,7 anni IQR 8,1-24,9. Il 56,6% era dislipidemico, il 37,8% iperteso e il 7% diabetico. Nove (3%) avevano avuto almeno un evento cardiovascolare maggiore. All'analisi logistica multivariata la dislipidemia è risultata associata ad ipertensione arteriosa (adjusted odds ratio, aOR 2,21, intervallo di confidenza, IC, 95% 1,25-3,88, p=0,006), precedente esposizione a inibitori della proteasi (PIs) (aOR 2,08, IC 95% 1,21-3,58, p=0,008), HIV-RNA rilevabile (aOR 1,90, IC 95% 1,11-3,26, p=0,019) ed età ≥50 anni (aOR 1,93, IC 95% 1,10-3,39, p=0,021). L' ipertensione arteriosa è risultata associata a dislipidemia (aOR 2.87, IC 95% 1.52-5.44, p<0.001), età ≥50 anni (aOR 2.62, IC 95% 1.31-5.23, p=0.006) e BMI >30 kg/m^2 (aOR 5,18, IC 95% 2,17-12,38, p<0,001). Il diabete mellito di tipo II è risultato associato all'ipertensione arteriosa (aOR 3.65, IC 95% 1.07-12.44, p=0.039).

Nei PLWH elevato BMI, età, alterazioni pressorie, lipidiche e glucidiche coesistono con esposizione a PIs e viremia rilevabile quali fattori di rischio per dislipidemia, ipertensione e diabete mellito.

Abstract

Non-AIDS-defining Illnesses are a rising challenge, foremost cardiovascular disease thanks to increase of the life expectancy of People Living With HIV (PLWH). Our aim was to describe the prevalence of cardiovascular risk factors and investigate predictors of blood hypertension, dyslipidemia, and diabetes mellitus type II in PLWH population. We conducted a retrospective cross-sectional study including PLWH followed in the Infectious Diseases Unit of Azienda Ospedaliera Universitaria Senese in 2020-2021.

Two-hundred and eighty-six PLWH were enrolled: 70% males, median age 54.4 interquartile range (IQR) 46.8-59.5, 33% smokers, with a median seropositive time of 14.7 years IQR 8.1-24.9. Among those 56.6% had dyslipidaemia, 37.8% hypertension and 7% diabetes mellitus. Nine (3%) PLWH had experienced of at least one major cardiovascular event. At multivariate logistic analysis blood hypertension (adjusted odds ratio, aOR 2.21, 95% confidence interval, CI 1.25-3.88, p=0.006), previous protease inhibitors (PIs) exposure (aOR 2.08, 95%CI 1.21-3.58, p=0.008), detectable HIV-RNA (aOR 1.90, 95%CI 1.11-3.26, p=0.019) and age ≥50 years (aOR 1.93, 95%CI 1.10-3.39, p=0.021) were associated with dyslipidaemia. Dyslipidaemia (aOR 2.87, 95%CI 1.52-5.44, p<0.001), age ≥50 years (aOR 2.62, 95%CI 1.31-5.23, p=0.006) and BMI >30 kg/m^2 (aOR 5.18, 95%CI 2.17- 12.38, p<0.001) were associated with blood hypertension. Blood hypertension was associated with diabetes mellitus type II (aOR 3.65, 95%CI 1.07-12.44, p=0.039). In PLWH high BMI, age, blood pressure, lipid and glucose alterations coexist with exposure to PIs and detectable viraemia as risk factors for dyslipidemia, hypertension and diabetes mellitus.

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Introduction

Nowadays due to increasing widespread availability of effective and well-tolerated combined antiretroviral therapy (cART), survival and quality of life in people living with HIV (PLWH) significantly improved. The increasing subset of older adults has a burden of non-communicable diseases (NCDs) similar to the general population but with a higher risk of age-related NCDs (1). Indeed, PLWH have an excess risk of cardiovascular disease (CVD) than people without HIV (2) with a driving mechanism that includes traditional and non-traditional risk factors (CVRF) (3). Non-traditional risk factors specific for PLWH included cART related mechanisms, affecting body weight and lipidic metabolism (4), although current therapies are less directly toxic than in early cART, and virus-related mechanisms (5), including pro-inflammatory status, CD4+ T-cell depletion, alteration of cholesterol metabolism and intestinal disorders. The traditional risk factors assumed peculiar patterns and epidemiology among PLWH and include smoking (6), body weight, familiarity, ageing (1), arterial hypertension (7), dyslipidemia (8) and diabetes mellitus type II (DM II) (9). In recent years many studies focused on the best predictive score to assess the risk of CVD. Researchers found that traditional risk charts designed for general population can underestimate the risk in PLWH (10) and lack specific scores designed in this setting (11). The burden of NCDs, especially CVD, directly affects morbidity, mortality, costs and needs to be investigated due to design a multi-disciplinary patient management for an early diagnosis and treatment of CVRF (12) including primary prevention strategies using lifestyle intervention and therapies (13; 14). Our study aims to describe the prevalence of cardiovascular risk factors and investigate predictors of blood hypertension, dyslipidemia and DM II in PLWH population in order to project a strategy to prevent CVD in PLWH.

Methods

We conducted a single centre retrospective observational cross-sectional study enrolling outpatients with a diagnosis of HIV infection, at least ≥18 years old, followed at the Infectious Diseases and Tropical Medicine Unit of University Hospital "Santa Maria alle Scotte", Siena, with at least one follow-up visit during 2020 and 2021.

Outpatient records were used to collect clinical and laboratory in an anonymized database. The following characteristics were collected: gender at birth, age, ethnicity, smoking attitude, height and weight, time of HIV positivity and time of antiretroviral treatment, use of antiretrovirals, risk factors for acquiring HIV infection, class of infection according to the Centre of Disease Control CDC Atlanta and coinfection with major hepatotropic viruses. Laboratory and clinical values related to HIV infection were collected: CD4 cells count at nadir and last visit, HIV-1 RNA at Zenith and last visit. The optimal immunological recovery (OIR) was defined as CD4 cells count ≥500 cells/μL with CD4 percentage ≥30% and CD4/CD8 ratio ≥1. Lipidic profile during the follow-up was investigated by the absolute value of triglyceride, total cholesterol with high-density lipoprotein (HDL) and low-density lipoprotein (LDL) fractions. Furthermore, we collected the last blood pressure measure, glycaemia, creatinine and estimated glomerular filtration rate (eGFR), which was calculated by CKD-EPI formula (Chronic Kidney Disease Epidemiology Collaboration). Antihypertensive, antidiabetics, lipid-lowering medicaments and current cART were registered at the last follow-up visit. Blood hypertension was defined as a Systolic Blood Pressure ≥140 mmHg and/or Diastolic Blood Pressure ≥90 mmHg or being under antihypertensive medicaments or a defined diagnosis of hypertension. Dyslipidaemia was defined as total cholesterol ≥200 mg/dL and/or LDL ≥160mg/dL or being under lipid-lowering medicaments or a defined diagnosis of dyslipidaemia. DMII was defined by two consecutives fasting blood glucose ≥126 mg/dL or glycohemoglobin (HbA1c) >6,5% or a positive Oral Glucose Tolerance Test (OGTT) or being under antidiabetics or a defined diagnosis of diabetes mellitus type 2. Additionally, we checked a positive anamnesis for major cardiovascular events (CVE), defined as acute myocardial infarction and stroke, and minor, defined as peripheral arterial disease, including haemodynamically relevant supra-aortic plaques, angina pectoris, heart failure, Transient Ischemic Attack, Deep Vein Thrombosis, Acute Pulmonary Embolism, arterial and/or coronary revascularization procedures.

Descriptive analysis and logistic regression analysis were performed to explore factors associated with a cardiovascular risk factor condition, defined

as hypertension, diabetes mellitus type II and dyslipidemia. In univariate analysis we investigate know predictors from the literature for cardiovascular risk factor conditions, variables with a *p value p <0,05* ("two tailed") was considered statistically significant and furthermore investigated in multivariate logistic regression (adjusted odds ratio, aOR, and corresponding 95% confidence interval, CI), correlations with a *p value p <0,05* ("two tailed") was considered statistically significant. The analysis was performed using software SPSS version 24.0 (SPSS Inc., Chicago, IL).

Results

Two-hundreds and eighty-six PLWH were included: the majority males, caucasian, experienced in cART treatment, with median age at the last follow-up of 54.36 years (IQR 46.80-59.54) and 190 (66.4%) were at least 50 years old. The risk factors for acquiring HIV infection were most sexual transmission in 30.7% (heterosexuals 17.1% and Male who have Sex with Males, (MSM), 13.6%). The median Body Mass Index (BMI) was 25 kg/m^2 (IQR 22.49-28.06). One third were smokers and 14.3% former smokers. The median years from the first HIV positive test was 14.67 (IQR 8.08-24.09); 21.7% in CDC class C. The median age at diagnosis was 35.02 years (IQR 28.02-43.78), the median viraemia zenith 44084 copies/mL (n=270 IQR 2340.75-199700) and the median CD4 cells count at nadir 262 cells/µL (n=285 IQR107-411). At the last follow-up the 22.4% had viraemia greater than 20 copies/mL with a median viral load in viraemic patients of 43.5 cp/mL (n=64 IQR 27-129.75). The median CD4 absolute count at the last follow-up was 666 cells/µL (n=285 IQR 464.25-900.5).

The median duration of cART in years was 12.27 (IQR 7.23-19.61), with almost one third had experienced treatment with abacavir, more than half with Protease Inhibitors (PIs), and almost all with nucleos(t)ide reverse transcriptase inhibitor (NRTI). The most used cART was two NRTI and one integrase inhibitor (INSTI) followed by two NRTIs and one non-nucleoside reverse transcriptase inhibitor (NNRTI) and an INSTI with an NRTI in dual regimen. The combinations of ART most used at the time of the last follow-up were BIC/TAF/FTC (28.7%), RPV/TAF/FTC (16.8%), DTG/3TC (10.1%), DRVc/TAF/FTC (7.3%), DTG/ABC/3TC (7%), DTG/RPV (3.5%). Detailed clinical and viro-immunological data are shown in **Table 1**.

Table 1. Clinical and viro-immunological characteristics.

CLINICAL AND VIRO-IMMUNOLOGICAL PARAMETERS (N=286)	
Median years from HIV diagnosis	14.67 (IQR[6] 8.08-24.09, MIN 1-MAX 38)
Naïve	10 (3.50%)
Median age at diagnosis of HIV positivity • >50 yo at diagnosis	35.02 (IQR 28.02-43.78, MIN 1-MAX 71) • 36 (12.60%)
Virological parameters	
• Median VL[1] zenith, cp/mL (N=270)	44084 (IQR 2340.75-199700, MIN 20-MAX 1000000)
Viral Load at last follow-up	• 163 (57%)
• VL negative or undetectable	• 59 (20.60%)
• VL detectable, but <20cp/mL	• 64 (22.40%)
• VL detectable ≥20cp/mL ◦ Median VL cp/mL in VL ≥20cp/mL subgroup (N=64)	43.50 (IQR 27-129.75, MIN 20-MAX 427000)
Immunological parameters	
• OIR[5] at last follow-up	206 (72%)
• Median nadir CD4, *cell/ µL* (N=285)	262 (IQR 107-411, MIN 1-MAX 1188)
◦ <200 *cell/ µL*	• 109 (38.20%)
◦ 200-499 *cell/ µL*	• 135 (47.40%)
◦ > 500 *cell/ µL*	• 41 (14.40%)
• Mediana CD4 at last follow-up, *cell/ µL* (N=285)	666 (IQR 464.25-900.50, MIN 23-MAX 1850)
HBsAg[3] positives	8 (2.80%)
HCV[4] positives	48 (16.80%)
HCV viraemic	1 (0.30%)
• Viral Load HCV (N=1) cp/mL	• 3210
Years in antiretroviral therapy	12.27 (IQR 7.23-19.61, MIN 1-MAX 37)
• <5 years	• 30 (10.50%)
• 5-10 years	• 85 (29.70%)
• 11-15 years	• 66 (23.10%)
• 16-20 years	• 39 (13.60%)
• >20 years	• 66 (23.10%)
Experienced with Abacavir	90 (31.30%)
• Median exposure years	3.5 (IQR 2-6, MIN 1-MAX 20)
Experienced with Protease Inhibitors	181 (62.90%)
• Median exposure *years*	8 (IQR 4-12, MIN 1-MAX 29)
Experienced with NRTI[2]	283 (99%)
Median exposure *years*	11 (IQR 7-18, MIN 1-MAX 37)
Antiretroviral therapy used at the last follow-up (N=284)	
2NRTI[2]+ INSTI[7]	124 (43.70%)
2NRTI+NNRTI[8]	52 (18.30%)
NRTI+INSTI	31 (10.90%)
2NRTI+ PIs[9]	25 (8.80%)
NNRTI+INSTI	12 (4.20%)
INSTI+PIs	10 (3.50%)
NNRTI+-PIs	8 (2.80%)
NRTI+PIs	6 (2.10%)
Others	16 (5.60%)
Last Switch reason in Experienced PLWH (N=274)	
Simplification	122 (44.53%)
Proactive Switch	68 (24.82%)
Toxicity	22 (8.03%)
Intensification	22 (8.03%)
Viral Failure [10]	17 (6.20%)
Drug-drug Interaction	9 (3.28%)
Pregnancy	3 (1.09%)
Immunological Failure	1 (0.36%)
Others	10 (3.65%)

[1] Viral Load; [2] Nucleoside/Nucleotide Reverse Transcriptase Inhibitors ;[3] Hepatitis B Virus Antigen; [4] Hepatitis C Virus; [5] Optimal Immunological Recovery (CD4 counts ≥ 500 cells/ µL, CD4 percentage ≥30%, CD4/CD8 ≥ 1); [6] Interquartile Range; [7] Integrase Strand Transfer Inhibitor, [8] Non-Nucleoside Reverse Transcriptase Inhibitor; [9] Protease Inhibitor; [10] two Viral Load ≥ 50 cp/mL or one ≥ 1000/mL or one ≥ 50 cp/mL after switch

LIPID METABOLISM, PRESSURE AND GLYCAEMIC PARAMETERS AT LAST FOLLOW-UP	
TOTAL CHOLESTEROL (median, mg/dL) (N=284)	190 (IQR[3] 167-218.75 MIN 95- MAX 322)
LDL[1] CHOLESTEROL (median, mg/dL) (N=217)	112 (IQR 91-138 MIN 35-MAX 255)
HDL[2] CHOLESTEROL (median, mg/dL) (N=218)	48 (IQR 41-60 MIN 25-MAX 117)
TRIGLYCERIDES (median, mg/dL) (N=280)	118 (IQR 81-164.5 MIN 37-MAX 525)
DYSLIPIDEMIA DIAGNOSIS (N=286)[4]	162 (56.6%)
USE OF ORAL LIPID-LOWERING AGENTS IN DYSLIPIDEMICS (N=162)	
• Diet and lifestyle	87 (53.70%)
• Statins	16 (9.90%)
• Ezetimibe	6 (3,70%)
• Statins+ Ezetimibe	4 (2.50%)
• Fibrate	9 (5.60%)
• Phytosterol	6 (3.70%)
• Omega3	13 (8.00%)
• Statins/omega3	4 (2.50%)
• Ezetimibe/fibrate	2 (1.20%)
• Ezetimibe/omega3	2 (1.20%)
• Statins/ezetimibe/omega3	2(1.20%)
• Fibrate/omega3	6 (3.70%)
• PSCK9[5] inhibitors /omega3	2(1.20%)
• Phytosterol/omega3	1 (0.60%)
• Fibrate/statins/omega3	1 (0.60%)
• Fibrate/omega3/phytosterol	
SYSTOLIC BLOOD PRESSURE (median, mmHg) (N=240)	120 (IQR[3] 110-130 MIN 90-MAX 170)
DIASTOLIC BLOOD PRESSURE (median, mmHg) (N=240)	75 (IQR 70-80 MIN 58-MAX 100)
BLOOD HYPERTENSION[6] (median, mmHg) (N=286)	108 (37.80%)
USE OF ANTIHYPERTENSIVES AGENTS IN HYPERTENSIVE PATIENTS (N=108)	
• Diet and lifestyle	24 (22.20%)
• Monotherapy	39 (36.10%)
• Dual Therapy	32 (29.70%)
• Triple Therapy	12 (11.10%)
• Quadruple Therapy	1 (0.90%)
GLYCAEMIA (median, *mg/dL*) (N=284)	93 (IQR[3] 85.25-101 MIN 65-MAX 264)
DIAGNOSIS OF DIABETES[7] (N=286)	20 (7%)
USE OF HYPOGLYCEMIC AGENTS IN DIABETICS (N=20)	
• Diet and lifestyle	6 (30%)
• Insulin	10 (50%)
• Metformin	3 (15%)
• GLP1[8] Agonist	1 (5%)

[1] Low Density Lipoprotein;[2] Hight Density Lipoprotein; [3] Interquartile Range; [4] LDL 160 mg/dL or lipid-lowering agents use or total Cholesterol 200 mg/dL or previous dyslipidemia diagnosis;[5] Proprotein of Convertase Subtilisin/Kexin type 9; [6] Systolic Blood Pressure ≥ 140mmHg or Diastolic Blood Pressure ≥ 90mmHg or use of antihypertensives agents or previous Hypertension diagnosis, [7] two fast glycaemia ≥ 126 mg/dL o glycated Haemoglobin ≥ 6.5% or glycaemia ≥ 200mg/dL after oral load of 75g glucose and symptoms or previous diabetes diagnosis; [8] Glucagon-like peptide 1

Table 2. Lipidic metabolism, blood pressure, and glycaemic parameters.

Dyslipidaemia was found in 162 individuals (56.6%) and 46,3% of these was used at least one lipid-lowering drug. Overall, 108 individuals (37.8%) had a diagnosis of arterial hypertension; of these, the majority were under antihypertensive therapy, most of them in combination therapy and only the 36.1% on monotherapy, the 22.2% were on treatment with dietary and lifestyle changes without any drugs. Twenty individuals (7%) had a diagnosis of DM II; 10 on insulin therapy. Median creatinine was 0.96 mg/dL (IQR 0.85-1.08) and the median estimated GFR was 84.7 mL/min/1.73 m2. According to GFR (stratified according to the guidelines of the American National Kidney Foundation) 38.5% had a normal renal function with a GFR of at least 90 mL/min/1.73 m^2. Nine subjects presented at least one major CVE, 7 an acute myocardial infarction (AMI) and 2 a stroke, with a median age from first detection of HIV infection of 16.12 years (IQR 8.93-26.83). In two cases there was a second major cardiovascular event (AMI) with a median time from HIV diagnosis of 18.94 years (IQR 15.01-18.94). Overall, 27 subjects experienced at least one minor CVE after a median of 14.66 years from HIV diagnosis (IQR 8.93-26.86). In 4 cases a second minor cardiovascular event followed, at a median distance from HIV diagnosis of 12.12 years (IQR 8.11-24.45) and in one case a third event after HIV diagnosis of 28 years. Details concerning lipid metabolism, blood pressure and glycemia are shown in **Table 2**.

Variables associated with Cardio vascular risk factors.

In multivariate logistic analysis, factors associated with dyslipidemia in PLWH were blood hypertension (aOR 2.21 95%CI 1.25-3.88, *p 0.006*), exposure to protease inhibitors (aOR 2.08, 95%CI 1.21-3.58, *p 0.008*), age greater than 50 years (aOR 1.93, 95%CI 1.10-3.39, *p 0.021*) and detectable viremia (aOR 1.90, 95%CI 1.11-3.26, *p 0.019*). There was an inverse correlation between HCV positivity and dyslipidemia (aOR 0.29, 95%CI 0.14-0.61 *p<0.001*) (**Figure 1**).

In multivariate logistic analysis, variables associated with blood hypertension were dyslipidemia (aOR 2.87, 95%CI 1.52-5.44, *p 0.001*), age greater than 50 years (aOR 2.62, 95%CI 1.31-5.23, *p 0.006*) and a BMI greater than 30 kg/m^2 (aOR of 5.18, 95%CI 2.17-13.38, *p<0.001*) (**Figure 2**).

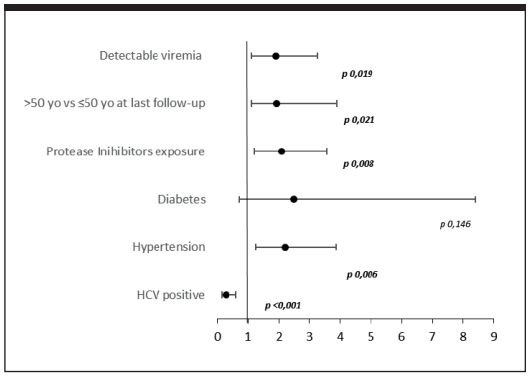

Figure 1. Variables associated with dyslipidemia.

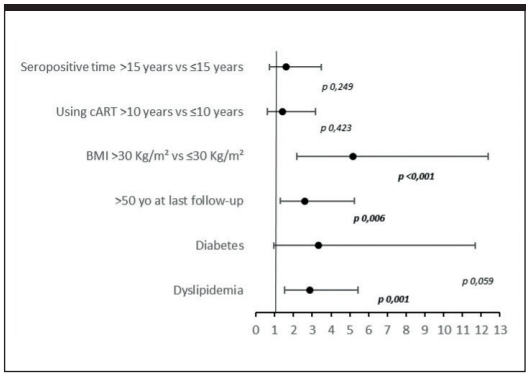

Figure 2. Variables associated with blood hypertension.

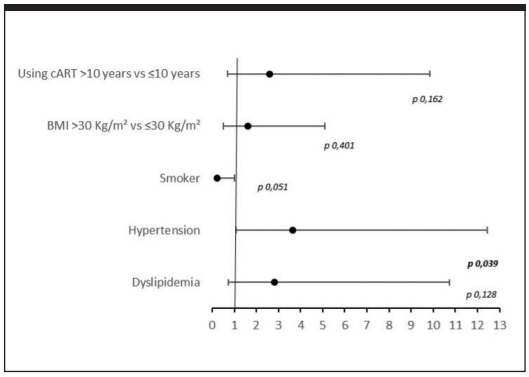

Figure 3. Variables associated with Diabetes Mellitus type 2.

In multivariate logistic analysis, arterial hypertension was associated with diabetes mellitus (aOR 3.65, 95%CI 1.07-12.44, *p 0.039*) (**Figure 3**).

Discussion

Currently in Western countries cardiovascular diseases are the leading cause of morbidity and mortality in PLWH, as in the general population, both due to aging and factors HIV specific, such as chronic inflammation and antiretroviral therapies (2).

Our study showed that the median age of the PLWH was 54.36 years, in agreement with recent studies which estimate that at least 50% of currently PLWH individuals in Western countries have an age greater than 50 years and non-infectious comorbidities in PLWHs are more precocious and more prevalent than in the general population (1).

Overall, the proportion of smokers is higher than the Italian median, 37.8% compared to 18.4% (15), suggesting how to quit smoking is essential in this setting (6).

As expected, due to the addition of traditional risk factors, such as age greater than 50 years, and those specific for PLWH, as prior PIs use and the presence of detectable viraemia, dyslipidemia is the most frequent CVRF (8).

Aging is a well-known risk factor related to alterations of the lipid profile through changes in the endothelium of the hepatic sinusoids, alterations in postprandial lipaemia, hormones and the activity of specific receptors (16). The association between hypertension and dyslipidemia is not only a cumulative risk but is reciprocal and synergistic in implementing cardiovascular risk, for underlying this concept was proposed in literature the term *"Lipitension",* in particular, hypertension is a risk factor for the development of dyslipidemia acting with a kidney and liver damage with subversion of endothelial and consequent alteration of renin-angiotensin-aldosterone and other hormones patterns (17). DMII is confirmed as a risk factor for the close interconnection between glucose and lipid metabolism, with qualitative and quantitative changes of lipoproteins in diabetic patients as known from the literature (18). The use of PIs, in particular first generation or boosting ritonavir (19), increases triglycerides and LDL both in PLWH and negative controls (20). Detectable viremia is also a risk factor for developing lipid profile alterations, confirming the role of chronic inflammation and the persistence of HIV in altering lipid metabolism, as suggested in the literature (21).

It is clear the need for lifestyle intervention, early screening of lipid alterations and the use, where necessary, of lipid-lowering drugs and switch to

less lipidic-impacting cART as suggested by recent Italian reviews (8).
In our study population, blood hypertension represented the second most prevalent risk factor, slightly higher than the Italian general population, 37.8% vs 31% (22) but in agreement with data from other cohorts of PLWH (23).
The age over 50 years, dyslipidemia and a BMI >30 kg/m^2 resulted as risk factors for the development of hypertension according to the literature (24). We found an inverse correlation between dyslipidaemia and HCV infection because we defined dyslipidemia as total cholesterol ≥200 mg/dL and/or LDL ≥160mg/dL; as known from literature, in people infected with HCV LDL-cholesterol is reduced because of the alteration of liver lipids metabolism, this reduction of LDL is not a protective against cardiovascular events and ,as well documented in literature, in HCV positive individuals the cardiovascular risk is greater than the general population (25). Managing blood hypertension looks fundamental; studies conducted on PLWH show that hypertension is associated with a higher risk of CVD, particularly for the development of AMI and strokes as underlined by meta-analysis (26) and several data from large cohorts (27; 28).
In agreement with other PLWH cohort findings, 7% of the enrolled were affected by diabetes mellitus (29). Blood hypertension emerged as a risk factor for DMII, confirming the role of hypertension in the development of diabetes mellitus as known in cohorts of PLWH (29) and non-infected people (30).

Limits and possible bias of the study

It should be emphasized that possible limits of our analysis are the low number of PLWH enrolled, the retrospective nature of the study and the monocentric origin of data. In particular we need studies that include more PLWH to investigate better the predictors for cardiovascular risk conditions, especially for the development of DMII due to the limited number of diabetics PLWH enrolled in our study.
Furthermore, even if dyslipidemia, DM II and blood hypertension are mutually and strictly interconnected, a possible bias of our analysis is the risk of reverse casualty between these cardiovascular risk conditions. Moreover, we analyse the exposure to different classes of cART but not all, at the time of the study the role of integrase inhibitors on BMI and consequent cardiovascular risk was not investigated, furthermore studies in this field are required. It's clear that the field of investigation is open and needs more research, preferably with multicentric and perspective studies.

Conclusion

Due to the effectiveness of cART and the higher age at diagnosis of HIV, in not-limited-resource-countries the age of PLWH is increasing. However, new infections are decreasing, and they are no longer exposed to the burden of AIDS-related diseases in terms of mortality and morbidity.
The burden of Cardiovascular Diseases has increased due to aging, the direct effect of chronic immune activation carried by the persistence of virus infection side effects of therapy, habits and lifestyle. In this setting, the prevalence of Cardiovascular Risk Factors and the incidence of cardiovascular diseases is higher and earlier than in the general population. Furthermore, peculiar risk factor has a strong effect other than general risk predictors. Although further investigations are needed to better understand the risk factors for the development of Cardiovascular Risk Factors and Cardiovascular Diseases, it is helpful to provide early focused screening, using risk assessment scales explicitly designed for PLWH integrating them with the classic assessment scales.
Moreover, it is mandatory to promote a healthy lifestyle and to treat hypertension and dyslipidemia pharmacologically, if necessary, paying attention to interactions with cART.
The global interventions to reduce and prevent Cardiovascular Risk Factors will be useful to improve the quality and expectancy of life in PLWH by reducing the multi-pathology burden and improving health indicators.

Other information:

A special memory by the authors should be reserved for the mourning Dr. Mauro Ruggeri, General Practitioner and tutor of the Specific Training Course on General Practice, Florence, attended by the first author of this study during the enrolling phase, who passed away in 2022. ■

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Bictegravir/emtricitabina/tenofovir alafenamide: dati real-life da un centro italiano.

Bictegravir/emtricitabine/tenofovir alafenamide: Real World Data in an Italian setting.

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Riassunto

Il ruolo della terapia antiretrovirale in singola compressa a base di Bictegravir/emtricitabina/tenofovir alafenamide (B/F/TAF) è ormai consolidato nella popolazione di soggetti che vivono con HIV, sia nei soggetti naive (TN) che già in trattamento antiretrovirale (TE).

I dati degli studi clinici randomizzati ci mostrano come questo regime abbia un'ottima efficacia e tollerabilità e la conferma ci arriva da alcuni studi osservazionali di coorte che hanno valutato efficacia, sicurezza, tollerabilità e gli esiti riferiti dai pazienti del trattamento con in persone con HIV TN o TE.

Da qui nasce il nostro studio retrospettivo che ha esaminato i dati real-life del nostro centro, l'ospedale Policlinico San Martino di Genova con l'obiettivo di valutare efficacia e tollerabilità di B/F/TAF in un'ampia coorte di soggetti che vivono con HIV, sia TN che TE, che hanno iniziato questo regime tra il 2020 e il 2022.

Abstract

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is an oral single-tablet regimen (STR) with the indication for the treatment -naïve (TN) and treatment-experienced (TE) people with HIV (PWH) with a limited drug interaction potential and a high barrier to resistance. We evaluated the effectiveness and tolerability of B/F/TAF in a large real-life cohort. This observational, retrospective, single-center, real-life cohort study included PWH who started B/F/TAF at our institution between 2020 and 2022. Virological success (VS) was defined as achieving an HIV-RNA <30 copies/ml six months after B/F/TAF start. We enrolled 475 PWH (48 TN, 427 TE); among the TE, 305 (71,4%) PWH had undetectable viremia at the time of initiation. After 6 months, 32 TN achieved virologic success, as did an additional 33 in TE group. CD4+ T-lymphocyte count increased, in TN group (from 353.8 to 612.8/µl). Fifty-six (11.7%) PWH discontinued treatment, only in one case due to therapeutic failure. Our data demonstrated that B/F/TAF is effective, safe, and durable for both TN and TE PWH.

Introduction

Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a single-tablet regimen (STR) recommended for HIV-1 antiretroviral therapy (ART) in treatment-naïve (TN) or treatment-experienced (TE) people living with HIV (PWH). (1,2) B/F/TAF has been evaluated in different randomized, double-blind, multicenter, non-inferiority trials (3,4), but few studies have assessed its effectiveness, tolerability, and safety in clinical practice (1-7). Given these premises, we analyzed the effects of B/F/TAF in our cohort.

Patients and methods

This was a retrospective cohort study conducted at Policlinico San Martino Hospital, Genoa, Italy, in which we enrolled all PWH who started a B/F/TAF-based regimen as of February 2020.

We performed a follow-up every 6 months, during which we analyzed HIV-RNA copies/mL and CD4+ T-cell lymphocyte count. The rate of change of these parameters was estimated at different time periods: 12 and 6 months before the start of B/F/TAF, at the start of B/F/TAF, and 6-12-18-24 months after starting B/F/TAF.

Data were collected from the paper and electronic medical records of the ONESYS Hospital Information System.

The reported laboratory values were extracted using the MEDINFO platform (www.reteligureHIV.it). Anthropometric, anamnestic, and laboratory data were collected for each patient: weight [kg], height [cm], BMI [kg/m^2], abdominal circumference [cm], sex, age, CDC stage, smoking, lipodystrophy, cardiovascular familiarity, date of HIV diagnosis, date of initiation of first ART, previous ART regimens with Integrase strand transfer inhibitors (INSTI), nucleoside reverse transcriptase inhibitor (NRTI), non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI), durability of ART regimens in months, chronic comorbidities and concomitant therapies, date of initiation of B/F/TAF therapy, and date of discontinuation for any reason.

Laboratory values considered were: HbsAg, HCV Ab, HCV-RNA, nadir CD4+ and its date, zenit HIV-RNA and its date, CD4+ T lymphocytes count, CD8+ T lymphocytes count and HIV-RNA.

This study aimed to assess the efficacy and tolerability of the B/F/TAF regimen for HIV.

Virological success has been defined as ≤30 copies/mL. T0 marked the start, and T1 was the 6-month value. We compared T0 and T1 to determine therapy-induced virological success in both experienced and naive groups.

Results

A total of 475 PWH, 427 TE, and 48 TN were included. Among the TE population, 78% had prior INSTI use (51% elvitegravir, 19% dolutegravir, and 8% raltegravir), while 10% used NRTIs, 9% PIs, and 2.8% NNRTIs. The median duration of ART in the TE group was 12.7 years. The population characteristics are shown in **Table 1**.

Among the 427 TE, 33 (8%) were detectable at the start of B/F/TAF and virological success was achieved. Among the 48 TN cases, 32 (67%) achieved virological success within the first 6 months. At month 6, six TN subjects were detectable, reducing to two by month 12. At 12 months, 430 (90%) PWH were undetectable.

Regarding the durability of the B/F/TAF regimen, 56 (11.7%) PWH discontinued treatment. Table 2 outlines the reasons for this, with 30 discontinuations due to missed follow-up.

Table 1. Patients' characteristics. TN, treatment naïve; TE, treatment experienced.

Variable	Overall	TN (48)	TE (427)
Mean age, years	49.2	38.1	50.4
Males, n (%)	319 (67)	32 (67)	287 (67)
Females, n (%)	156 (33)	16 (33)	140 (33)
Height, cm	170.3	169.2	170.4
Familiarity for cardiovascular disease	83 (17)	10 (21)	73 (17)
Current smokers	236 (50)	21 (44)	215 (50)
HbsAg positive	21 (4)	0	21 (5)
HCV-Ab positive	122 (26)	1 (2)	121 (28)
Detected HCV-RNA	11 (2)	0	11 (3)
Lipodystrophy	64 (13)	1 (2)	63 (15)
AIDS (Stage C of CDC classification)	50 (10)	6 (13)	44 (10)
Nadir CD4+ T lymphocytes/µl	257.5	339.9	247.1
Zenit HIV-RNA /ml	445516.1	939197.2	383806
Years since HIV diagnosis	14.1	0.1	15.7
Years of antiretroviral therapy	11.3	0	12.7

However, it is important to note that only one PWH experienced treatment failure, demonstrating the effectiveness of the B/F/TAF-based regimen.

Statistical analysis of the data collected using the LIFETEST procedure made it possible to construct a Kaplan–Meier curve (**Figure 1**) to examine discontinuation from the study and therefore from B/F/TAF therapy.

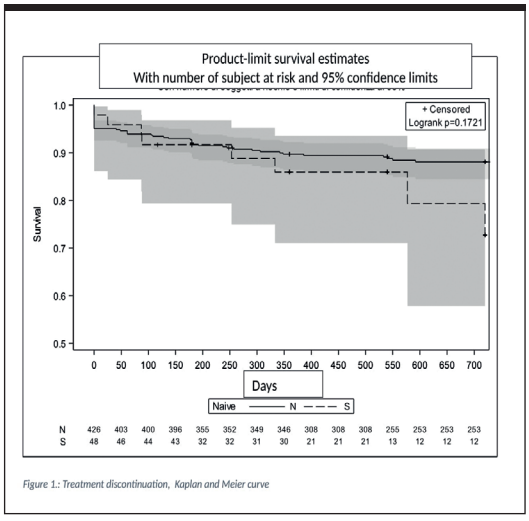

Figure 1. Durability of B/F/TAF by Kaplan - Meier estimates

Discussion

Our primary endpoint was to evaluate the effectiveness and tolerability of B/F/TAF, a once-daily fixed-dose ART regimen approved for PWH treatment.

At six months, 364 (77%) PWH achieved virological suppression, which increased to 430 (90%) at 12 months.

Reasons for discontinuation	TE		TN	
	N	%	N	%
Allergy	1	0.21	1	0.21
Self-discontinuation	1	0.21	0	0
Change of center	5	1.05	0	0
Death	5	1.05	0	0
Failure	1	0.21	0	0
Pregnancy	2	0.42	0	0
Interactions with other therapies	1	0.21	1	0.21
Intolerance	2	0.42	0	0
Other pathology	2	0.42	0	0
Lost to follow-up	30	6.32	4	0.84

Table 2. Reasons of discontinuation.

TN had a higher success rate (66%) than TE (10%) within 6 months. CD4+ T-cell count consistently increased, notably within the first 6 months.

Therefore, this study highlights the efficacy of B/F/TAF in achieving virological success and boosting CD4+ T cell counts, especially during the initial treatment phase.

It should be noted that, as expected, the increase in CD4+ lymphocytes was more pronounced in TN (from 353.8 to 612.8/µl) than in TE (from 664.2 to 685.6/µl). As shown in a recent Quebec cohort study (8), INSTI-based ART appears to be better than NNRTI- and PI-based regimens for normalizing the CD4+/CD8+ ratio, a potential marker of reduced immune system activity.

The two-year drop-out rate was 11.7%, with only one case of therapeutic failure, confirming the effectiveness of this STR regimen.

Conclusion

After 24 months of analysis, B/F/TAF demonstrated its efficacy, as evidenced by the achievement and maintenance of an HIV-RNA load below 30 copies/mL in 90% of PWH and an increase in CD4+ T-lymphocyte count. In addition, the low dropout rate is evidence of good tolerability, which translates to a high level of adherence in clinical practice. ■

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Aggiornamenti da EACS2023 sulle malattie cardiovascolari e sul trattamento con farmaci long-acting nelle persone con HIV.

Update from EACS2023 about cardiovascular diseases and long-acting treatment in people living with HIV.

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Riassunto

L'avvento della terapia antiretrovirale a lunga durata d'azione (LA ART) ha segnato un'avanzata significativa nella gestione dell'HIV, rendendolo una condizione cronica gestibile. Nonostante ciò, le persone viventi con l'HIV (PWH) si confrontano con la gestione delle comorbidità che incidono sulla loro qualità di vita. Il presente manoscritto fornisce un aggiornamento sulla gestione delle comorbidità nell'era della LA ART, riflettendo sui dati e sui progressi esposti durante l'EACS 2023. Tra gli argomenti trattati ci sono gli effetti cardiovascolari del passaggio al dolutegravir, l'efficacia dei modelli di valutazione del rischio cardiovascolare e l'evoluzione delle condizioni cognitive e della fragilità nelle PWH. Studi selezionati hanno mostrato che il cambio al dolutegravir non aumenta il rischio cardiovascolare rispetto agli inibitori della proteasi e che nuovi modelli di valutazione rischio cardiovascolare hanno mostrato maggiore accuratezza rispetto ai modelli più vecchi. Interventi mirati hanno portato a miglioramenti cognitivi, sottolineando il valore di servizi di cura specializzati. Inoltre, è stata evidenziata la prevalenza e la progressione della fragilità nelle persone anziane viventi con l'HIV. Il trattamento con cabotegravir e rilpivirine a lunga azione ha dimostrato alta efficacia e tollerabilità, con tassi bassi di fallimento virologico, sostenendo l'efficacia di tali regimi nel passaggio da studi controllati alla pratica clinica quotidiana. Tuttavia, la gestione degli effetti collaterali e le rare reazioni allergiche richiedono un attento monitoraggio e supporto al paziente, soprattutto nelle fasi iniziali della terapia. La ricerca evidenzia la necessità di modelli di cura che integrino valutazioni geriatriche e affrontino le comorbidità per migliorare il benessere generale delle PWH. Questi dati rafforzano la posizione della LA ART come opzione di trattamento praticabile e preferita, capace di offrire un approccio conveniente e centrato sul paziente per la gestione dell'HIV.

Abstract

The management of HIV has significantly evolved with antiretroviral therapy (ART), especially with the introduction of long-acting (LA) regimens such as cabotegravir and rilpivirine. However, as people living with HIV (PWH) age, comorbidities become a central concern in treatment and management strategies, impacting their quality of life.

An review of the latest research findings from EACS 2023 was conducted, highlighting advancements and current trends in HIV treatment, particularly addressing the interplay between long-term ART, comorbidities, and quality of life. The conference presented studies on the cardiovascular implications of switching to dolutegravir, the effectiveness of different cardiovascular risk assessment models, the cognitive trajectories in PWH following clinical interventions, and the transitions of frailty in an aging HIV-positive population.

The shift to dolutegravir showed no significant difference in cardiovascular risk compared to protease inhibitors.

Discrepancies in cardiovascular risk assessments suggest the need for HIV-specific models.

Cognitive improvements were noted following comprehensive interventions, emphasising the benefits of specialised services. The prevalence of frailty and associated factors like low CD4 counts and Type 2 diabetes were highlighted, calling for geriatric principles in HIV care. In conclusion, LA treatments like cabotegravir and rilpivirine demonstrate high efficacy and tolerability in real-world settings, with low virologic failure rates.

The data underscore the necessity of integrating geriatric care and addressing comorbidities to improve the overall well-being of PWH.

Future strategies should focus on personalised care that aligns with patient preferences and lifestyles, considering the psychological, cognitive, and physical aspects of health.

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Introduction

The management of Human Immunodeficiency Virus (HIV) has undergone significant evolution over the past two decades, transforming HIV from a fatal disease into a manageable chronic condition. This transformation has largely been due to the advent of effective antiretroviral therapy (ART), which has not only improved the longevity of people living with HIV (PWH) but also played a crucial role in public health by reducing the transmission rates of the virus (1–3).

While ART has significantly improved life expectancy, PWH now face the challenge of managing comorbidities that can arise as a result of long-term HIV infection and ART exposure (4). These comorbidities, including cardiovascular diseases, metabolic disorders, bone density abnormalities, renal and liver diseases, and certain cancers, compound the management challenges and can significantly impact the quality of life of PWH (1,5–8). Furthermore, mental health disorders such as depression and anxiety are prevalent among PWH, adding another layer to the complexity of HIV management (9).

Quality of life for PWH is not only influenced by physical health but also by psychosocial factors, including stigma, social support, and mental well-being (10). As the population of PWH ages, the burden of these comorbidities is expected to increase, necessitating a shift in treatment strategies from not only prolonging life but also improving the quality of life (11–13).

In the quest to enhance the quality of life, long-acting (LA) antiretroviral treatments represent a groundbreaking advancement. The combination of cabotegravir and rilpivirine, administered as two-month injections, has emerged as a promising alternative to daily oral regimens, addressing key challenges related to adherence, convenience, and the psychological burden of daily medication (14). This shift has the potential to provide a sense of liberation from the constant reminder of their condition, thereby improving the overall well-being and quality of life for PWH. The advent of such long-acting therapies signifies a major leap forward in HIV treatment paradigms, offering not just clinical benefits but also aligning with the preferences and lifestyles of PWH. It is a reflection of the personalised care approach that is increasingly becoming the focus of HIV management strategies.

This manuscript aims to provide a comprehensive update regarding the management of comorbidities in the era of long-acting antiretroviral therapy, with a special focus on the insights and advancements presented at the latest European Conference on HIV/AIDS (EACS 2023), held in Warsaw from 18 to 21 October. The discussions and findings from this conference shed light on current trends, challenges, and future directions in the treatment of HIV, particularly in how we approach the complex interplay between comorbidities, long-term therapy, and quality of life.

Comorbidities

Several studies have been presented in the past EACS conference. We selected the most interesting papers.

MeP.T3.03 - Change in blood pressure, weight and other cardiovascular disease risk factors after switch to dolutegravir versus staying on a protease inhibitor; post-hoc analysis of the 48-week randomised 2SD trial

Loice Achieng Ombajo et al. presented a study entitled “Change in blood pressure, weight and other cardiovascular disease risk factors after the switch to dolutegravir versus staying on a protease inhibitor; post-hoc analysis of the 48-week randomised 2SD trial” (15). The authors explored the effects of switching to dolutegravir (DTG) on cardiovascular risk factors in HIV-positive individuals. This post-hoc analysis from the Second-line Switch to DTG study (2SD) assessed changes in blood pressure, weight, incident hypertension, and diabetes, along with alterations in the Atherosclerotic Cardiovascular Disease (ASCVD) risk prediction score over 48 weeks. The study involved 795 black participants, the majority of whom were female, and found that while DTG was associated with a higher degree of weight gain, there was no significant difference in the onset of hypertension, variations in blood pressure, or overall cardiovascular risk between the DTG group and those who continued on protease inhibitors. The study concluded that despite the weight gain linked to DTG, the treatment did not increase the risk of hypertension or overall cardiovascular risk compared to protease inhibitors. These findings are particularly relevant for clinicians considering DTG as a switch option for their patients, underscoring the importance of monitoring cardiovascular health

and individual risk factors when making therapeutic decisions in the management of HIV.
The findings of this study add to the growing body of evidence regarding the metabolic and cardiovascular implications of DTG therapy. The lack of significant difference in hypertension incidence and blood pressure changes is reassuring for clinicians considering DTG as a switch option for their patients. However, the associated weight gain with DTG is an important consideration, especially as weight gain can be a risk factor for other health complications over time (16). This analysis highlights the need for individual risk assessment when making treatment decisions, considering the potential for weight gain with DTG and its implications for cardiovascular health. However, The median age of participants in the study was 46 years, signalling a gap in data regarding the older HIV-positive population who may be at a heightened risk for cardiovascular disease. This gap underscores the necessity for further studies that focus specifically on older individuals living with HIV.

eP.B2.012 - Cardiovascular risk assessment with SCORE, SCORE2 and D:A:D in people living with HIV with high prevalence of cardiovascular risk factors

In this interesting study, entitled **"Cardiovascular risk assessment with SCORE, SCORE2 and D:A:D in people living with HIV with high prevalence of cardiovascular risk factors"**, Maria Joao Miguel et al. evaluated the effectiveness of three CVD risk prediction models (the D:A:D (Data Collection on Adverse Events of Anti-HIV Drugs) specific to HIV, the SCORE (Systematic COronary Risk Evaluation) for the general European population, and its updated version, SCORE) (17). The retrospective analysis included data from 42 patients attending a CVD risk clinic tailored for PWH. The median age of this cohort was 60 (IQR 52-66) years. In addition, a significant proportion of the cohort had obesity, hypertension, dyslipidemia, diabetes, and smoking habits, alongside HIV-specific risk factors such as low CD4 nadir, exposure to protease inhibitors, current use of integrase inhibitors, and abacavir.
The findings showed that the risk of CVD was classified as high or very high in a larger proportion of patients when using the SCORE2 and D:A:D models compared to the original SCORE model.
The agreement between the predictions of SCORE2 and D:A:D was greater than that between SCORE and D:A:D. This discrepancy in risk assessment suggests that the older SCORE model might underestimate the CVD risk in PWH, a group already known to have a unique risk profile due to both HIV-specific factors and antiretroviral therapy.
These results highlight the limitations of traditional CVD risk assessment tools in accurately predicting risk in PWH and the potential need for models that better account for the specific risk factors associated with HIV. With the high discordance in predicted CVD risk among the three models, especially in a population with a high burden of traditional and HIV-specific CVD risk factors, there's a clear call for improved CVD risk assessment tools. Such tools would need to integrate the unique aspects of HIV pathology and treatment to provide accurate risk stratification and guide clinicians in optimising preventive strategies for this vulnerable population.

eP.B2.016 - Cognitive trajectories among people with HIV attending a dedicated memory clinic for people living with HIV

Samuel Rhodes et al. Presented a study entitled "Cognitive trajectories among people with HIV attending a dedicated memory clinic for people living with HIV" to explore the management and progression of cognitive impairment (CI) in individuals living with HIV (18). The researchers focused on patient-centered clinical interventions to manage factors traditionally associated with CI, with an aim to maintain or improve cognitive performance over time.
The interventions provided by the clinic were comprehensive, including referrals to mental health services and social support services, reviews and modifications of antiretroviral therapy (cART), assessment of non-ART co-medications, and cognitive remediation. Results indicated an overall trend of improvement in global cognitive performance, with significant gains noted in the domains of delayed memory and executive function. Out of 136 patients, 38 had clinically indicated reassessments, most of whom were male and white, with a median age of 56 years.
Most of these patients had an undetectable viral load at the time of reassessment. The study concludes that in the observed cohort, cognitive performance either remained stable or improved for

the majority of PWH following the patient-centered interventions. This finding highlights the potential benefits of holistic and tailored approaches to managing cognitive impairment in HIV, reinforcing the importance of specialised care services like the Orange clinic.

Reading this study, it is evident that dedicated cognitive care, tailored to the needs of PWH, can play a crucial role in managing and potentially improving cognitive outcomes. The improvement seen in specific cognitive domains suggests that targeted interventions, alongside routine HIV care, may enhance cognitive health. However, it also prompts further research into the specific types of interventions that are most effective and the long-term sustainability of cognitive gains in this population. Multidisciplinary care models that address both the medical and psychosocial aspects of living with HIV are crucial for the comprehensive care of this group.

eP.B2.137 - One-year frailty transitions among persons living with HIV aged 70 years or more on ART

Jannette Achour et al. presented a study entitled "One-year frailty transitions among persons living with HIV aged 70 years or more on ART" about the prevalence and progression of frailty among older PWH (19). The study aimed to assess the frequency and factors associated with frailty transitions over a one-year period in PWH aged over 70 on ART within the French multicenter ANRS EP66 SEPTAVIH study. It included 508 PWH, with 491 analysed after excluding 17 who died before the 12-month mark. Frailty was assessed at baseline and after 12 months, categorising participants as robust, prefrail, or frail. Logistic regression models adjusted for gender, age, education, and period of HIV diagnosis were employed to evaluate factors associated with transitions in frailty states, with multiple imputations used for missing data.

The study findings revealed that over a twelve-month follow-up, 18% of participants experienced a worsening in their frailty level, while 14% showed improvements in their functional capacities.

There was a noted relationship between immunological status, specifically CD4 cell count, and frailty, where a CD4+ T-cell count below 350/mm3 indicated premature aging of the immune system in PWH. Additionally, Type 2 diabetes emerged as a factor associated with the transition from prefrailty to frailty, highlighting metabolic dysfunction and chronic inflammation as contributing to the deterioration of muscle and nerve functions characteristic of frailty. Moreover, men were less likely to recover from frailty to prefrailty than women.

This study highlights the urgent need to integrate geriatric principles into HIV care. Given the complex interplay between HIV, its treatments, and age-related comorbidities, geriatric assessments, including frailty screening, should become routine. Encouraging exercise to combat sarcopenia and potentially reverse prefrailty could be a key component of care for older PWH. These insights underscore the need for a multidisciplinary approach to the care of older adults with HIV, addressing the full spectrum of their healthcare needs.

eP.B2.136 - Neurocognitive impairment, and anxiety symptoms may influence the development of prefrailty/frailty in Japanese people living with HIV aged over 40 years

Hideta Nakamura et al. conducted a study entitled "Neurocognitive impairment, and anxiety symptoms may influence the development of prefrailty/frailty in Japanese people living with HIV aged over 40 years" that addresses the growing concern of frailty among the ageing of PWH in Japan (20). The objective of the study was to determine the prevalence of frailty and identify contributing factors among male Japanese PWH aged 40 or older who have been on ART for at least a year.

In this cross-sectional analysis, participants were assessed for frailty using the Fried frailty assessment and other tools such as the Short Performance Physical Battery (SPPB), Generalized Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), and the Japanese version of the Montreal Cognitive Assessment (MOCA-J). The study analysed data from 126 participants and found that 11.9% were frail and 61.9% were prefrail. Weight loss and exhaustion were the most common markers of frailty.

The results showed that several factors were significantly associated with frailty and prefrailty, including lower BMI, current smoking status, the presence of multiple comorbidities, polypharmacy, current CD4 T-cell count, and lower scores on the SPPB, GAD-7, PHQ-9, and MOCA-J. Notably, anxiety (GAD-7 ≥10)

First Author	Country	Number of Patients	Virological Failures	Developed Resistance	Treatment Interruptions	Other Findings
Rubenstein E. (22)	France	72	1 (1.4%)	Not specified	5 (4.2%)	Association of low cabotegravir trough levels with high BMI and absence of oral lead-in.
Deschanvres C. (24)	France	1134	14 (1.1%)	4/6	80 (7.1%)	The virologic failure rate aligns with clinical trials, emergence of resistance mutations in some cases.
Jonsson-Oldenbüttel C. (26)	European	430	1 (0.23%)	Not specified	Not specified	High acceptability and comparable feasibility of the regimen's implementation across different countries.
Mazzitelli M. (27)	Italy	65	1 (1.5%)	0	5 (7.7%)	Decrease in reported side effects from 9.2% to 63.3% at 12-week follow-up, neutral impact on immunological, inflammatory, and metabolic parameters.

Table 1. Characteristics of the four posters presented at EACS2023 about the Long-Acting treatment with Cabotegravir-Rilpivirine.

and cognitive impairment (MOCA-J ≤25) were both found to be significant in multivariate analysis, suggesting they may play a critical role in the onset of frailty. The authors suggest that addressing mental health and cognitive function could be key strategies in reversing frailty status in this demographic. However, they also indicate that further research is needed to clarify the clinical features of frailty in senior Japanese PWH and to develop effective interventions.

About their findigns it is evident that the intersection of mental health, cognitive function, and frailty presents a complex challenge in the care of older PWH. Given the high prevalence of prefrailty and the significant associations with anxiety and cognitive impairment, it becomes crucial to integrate mental health and neurocognitive evaluations into routine clinical care for PWH. Early identification and intervention for anxiety and cognitive impairment may offer potential pathways to mitigate the progression of frailty and enhance the quality of life for older adults living with HIV. (19,21) These results underline the importance of a holistic approach to the health of PWH, taking into account not only the physical but also the psychological and cognitive dimensions of well-being.

In conclusion, reading these studies, it is evident that comorbidities in PWH present a multifaceted challenge requiring comprehensive and tailored approaches. Collectively, these studies illuminate the evolving landscape of HIV care, extending beyond viral suppression to addressing the broader determinants of health and well-being. They advocate for a holistic care strategy that not only treats HIV but also proactively manages the complex array of comorbidities associated with aging in this population. As we look to the future, it is imperative that HIV care models adapt to meet these needs, ensuring that PWH can not only live longer but also with a higher quality of life.

Long-acting treatments

Several studies have been presented at the EACS2023 conference. We selected four of them for this review (**Table 1**).

B1.036 - Low cabotegravir trough concentrations without oral lead-in in patients with HIV-1 infection switching to long-acting cabotegravir and rilpivirine

Rubenstein et al. presented a poster entitled "Low cabotegravir trough concentrations without oral lead-in in patients with HIV-1 infection switching to long-acting cabotegravir and rilpivirine" (22). In this work the authors presented the findings from a study conducted in two French HIV clinics from March 2022 to April 2023. The study aimed to assess the efficacy, safety, and drug trough concentrations of LA cabotegravir (CAB) and rilpivirine (RPV) in patients with virologically-suppressed HIV-1 who were switching to this LA treatment. They included 72 participants, with a median age of 30.4 years, mostly male (84.7%), and a median BMI of 24.2 kg/m^2. The participants were mainly from Europe (65.3%), and the majority were men who have sex with men (MSM), at 70.8%. The median of follow-up was 15 months, and there was one case of virologic failure (1.4%) where the patient had a BMI of 29.4 kg/m^2, did not receive an oral lead-in, and had plasma HIV-1 RNA levels at 2820 copies/mL at one month.

The data indicated that low cabotegravir trough levels were associated with high BMI at one month and the absence of an oral lead-in at both one and three months. No significant risk factor was identified for rilpivirine. The median trough levels of CAB were below the defined low levels at both one and three months, and a significant proportion of participants had CAB levels below the protein-adjusted 90% inhibitory concentration (PAIC90). However, the elimination half-life of oral CAB and RPV is 41 and 45 hours, respectively (23). It is not clear how it could have an impact on the concentration after one and three months. Further study would be necessary in order to understand better this aspect.

MeP.T2.01 - Cabotegravir-rilpivirine long acting: data in real life setting in a large French cohort

Deschanvres et al. Conducted a study entitled "Cabotegravir-Rilpivirine Long-acting: Data in real-life setting in a French Cohort" which includes 23 HIV centers and more than 65 thousand PWH (24).

They included in this study all PWH who were switched to LA CAB+RPV, with the aim to assess the efficacy and tolerability of the treatment and to describe instances of viral failure in a real-life setting. Overall, they included 1134 subjects, of whom 80 (7.1%) discontinued the treatment. The virologic failure occurs in 14 (1.1%) of patients. Among the 6/14 genotypes available at the time of virologic failure, 4 showed the emergence of resistance-associated mutations. The main reasons for discontinuation were adverse events (25, 2.2%), and patients' decision (21, 1.8%). In conclusion, the study demonstrated high efficacy and tolerability of LA CAB+RPV treatment in a real-life setting, confirming those observed in Phase 3 studies. The observed virologic failure rate (1.1%), aligns closely with the rates reported in clinical trials (14,25). The emergence of resistance-associated mutations in the event of treatment failure is a point of concern, underscoring the importance of adherence to treatment and regular monitoring. The fact that most discontinuations occurred within the first three months suggests that the early treatment initiation phase is critical, and patients may require additional support during this period. Although not specified in the quotes provided, the side effects leading to discontinuation would be an important factor to consider in clinical practice, as they impact patients' quality of life and willingness to continue treatment.

eP.A.101 - Efficacy, safety and implementation outcomes of Cabotegravir + Rilpivirine long-acting by country in the Cabotegravir And Rilpivirine Implementation Study in European Locations (CARISEL)

Celia Jonsson-Oldenbüttel et al. presented the results of a Phase 3b implementation study. The study examined PWH across Belgium, France, Germany, Spain, and the Netherlands, which received LA CAB+RPV every two months (26). The CARISEL study was specifically designed to evaluate the perceived acceptability, appropriateness, and feasibility of CAB + RPV LA implementation for staff and study participants. Clinics without prior experience with administering CAB + RPV LA were preferentially selected to ensure a diverse participant group broadly representative of PWH in Europe. The key outcomes demonstrated high effectiveness, with 81-94% of participants maintaining HIV-1 virologic suppression at 12 months and a confirmed virologic failure (CVF) rate of only 0.23%. The study also found CAB + RPV LA to be well-tolerated, increasing participant satisfaction irrespective of the country, and observed high and comparable acceptability, appropriateness, and feasibility of the regimen's implementation across all countries involved.

Of the 430 participants who received CAB + RPV LA, the median age was 44 years, with 25% female at birth and a median BMI of 25 kg/m^2. The study noted that 13 of 18 clinics (72%) had no experience administering CAB + RPV LA at the start of the study. Safety data indicated that drug-related Grade ≥3 adverse events (AEs) occurred in ≤5% of participants across all countries, except for France (11%), which was largely driven by injection site reactions (ISRs). AEs leading to treatment withdrawal ranged from 6–17% across countries. ISRs were the most common AE reported, with most being Grade 1 or 2 in severity and having a median duration of 3–4 days. Discontinuations due to injection-related reasons ranged from 3–15% across countries, with over half occurring due to injection site pain. Participant satisfaction with CAB + RPV LA treatment was high at baseline. It improved across every country, as measured by the HIV Treatment Satisfaction Questionnaire status version (HIVTSQs), with mean increases ranging from +1.60 to +4.21 at month 12. These results are significant as they corroborate the effectiveness of CAB + RPV LA as observed in

controlled clinical trials and demonstrate successful implementation in a real-world setting across different European countries (14,25).
The very low CVF rate supports the reliability of this treatment in diverse populations.
The high satisfaction and acceptability scores suggest that patients find the two-month dosing regimen preferable to daily oral therapy, likely contributing to better adherence and overall treatment success.
The findings underscore the importance of considering patient perspectives and implementation outcomes when introducing new treatment regimens in clinical practice.

eP.A.075 - Real life data on clinical and laboratory outcomes of long-acting cabotegravir and rilpivirine in people with HIV

Mazzitelli et al., in this study entitled "Real life data on clinical and laboratory outcomes of long-acting cabotegravir and rilpivirine in people with HIV", presented the preliminary real-life experiences with LA CAB-RPV (27).
The study included 65 PWH, with 73.8% being male, a median age of 48 years, and 63% being men having sex with men (MSM). At 12 weeks of follow-up, 92.3% retained the LA regimen with undetectable HIV-RNA. Five (7.7%) participants discontinued the regimen due to various reasons, including one for virological failure without resistance mutation development, three for severe pain, and one for allergic reaction. The most common side effects reported were pain and myalgia, but the proportion of participants who did not report any side effects increased significantly from baseline to the last point of follow-up (9.2% to 63.3%).
Immunological, inflammatory, and metabolic parameters measured at baseline and at the 12-week follow-up showed no significant changes, suggesting a neutral effect of the LAIC/R regimen on these parameters.
These results provide valuable insights into the use of LA CAB+RPV in a real-life clinical setting. The decrease in side effects over time is encouraging and could indicate that patients may adapt to the treatment. However, the occurrence of severe pain and allergic reactions, leading to discontinuation for some, underscores the need for careful patient monitoring and management of side effects.
The fact that a significant proportion of patients chose this treatment themselves suggests a preference for LA regimens, possibly due to the convenience and reduced pill burden compared to daily oral therapies.
The neutral impact on immunological, inflammatory, and metabolic parameters is reassuring and supports the long-term sustainability of this treatment option.
In conclusion, the four studies presented provide a comprehensive overview of the real-world application of long-acting cabotegravir and rilpivirine (LA CAB+RPV) in people with HIV.
These studies affirm the effectiveness and tolerability of LA CAB+RPV, mirroring the positive outcomes seen in clinical trials.
A notable finding across these studies is the sustained virologic suppression achieved by most participants, with exceptionally low virologic failure rates.
This suggests that the benefits of long-acting regimens translate effectively from controlled trial settings to everyday clinical practice.
Despite the overall success of LA CAB+RPV, challenges such as the management of side effects, particularly injection site reactions, and the rare instances of severe pain and allergic reactions leading to treatment discontinuation, highlight the need for vigilant monitoring and patient support, especially during the initial stages of therapy.
Patients' preferences underscore the importance of personalised care for this treatment, indicating the value placed on reduced dosing frequency and the potential for increased adherence.
However, further research is needed, particularly in understanding the pharmacokinetics of long-acting formulations and the factors influencing drug trough concentrations over time.
Overall, these real-life data reinforce the position of LA CAB+RPV as a viable and preferred treatment option for PWH, capable of offering a convenient and patient-centred approach to managing HIV. With the growing emphasis on patient satisfaction and treatment personalisation, LA CAB+RPV stands as a testament to the progress in HIV therapy, signifying a shift towards regimens that accommodate the lifestyles and preferences of those they are designed to help. ■

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Meningite da Escherichia Coli in una persona con infezione da HIV; descrizione di un caso clinico e revisione della letteratura.

Escherichia Coli meningitis in a person living with HIV infection: a clinical case and review of the literature.

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Riassunto

La meningite da *Escherichia* coli è rara negli adulti; è diagnosticata occasionalmente come complicanza di infezioni delle vie urinarie o di procedure neurochirurgiche e traumi cranio-facciali associata a fattori di rischio come diabete mellito, alcolismo, neoplasie e deficit immunitari.
Descriviamo il caso clinico di un paziente sieropositivo per HIV-Ab, ricoverato presso la Divisione di Malattie Infettive del nostro ospedale per cefalea frontale, febbre e diarrea presenti da circa due settimane.
La rachicentesi eseguita all'ingresso poneva diagnosi di meningite da E.coli toti-S; positive per lo stesso germe risultavano anche tutte le emocolture. Veniva impostata terapia antibiotica con ceftriaxone con rapido miglioramento del quadro clinico.
Durante la degenza veniva, inoltre, posta diagnosi di adenocarcinoma del retto con linfadenopatia satellite con indicazione chirurgica.

Abstract

Meningitis caused by Escherichia coli is rare in adults, occurring as a sequela of urinary tract infection or a complication of neurosurgery and craniofacial trauma; other risk factors are diabetes mellitus, alcoholism, neoplasms and immunocompromised states.
We describe the clinical case of a person with HIV infection, admitted to our Infectious Disease department for fever, headache, and diarrhea present for two weeks. Examination of CSF demonstrated presence of E. coli toti-S; all blood cultures were positive for the same gram-negative bacillus.
The clinical condition rapidly improved with administration of ceftriaxone.
During his recovery, we also made a diagnosis of a rectal adenocarcinoma, with indication for surgery.

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La meningite da *Escherichia* coli è rara negli adulti; diagnosticata occasionalmente come complicanza di infezioni delle vie urinarie o di procedure neurochirurgiche e traumi cranio-facciali (1), è associata a fattori di rischio come diabete mellito, alcolismo, neoplasie e deficit immunitari. Il tratto gastrointestinale è una possibile fonte di batteriemia da *E. coli*; la traslocazione gastrointestinale è infatti implicata nell'insorgenza di meningiti a esordio tardivo nei neonati (2).
L'infezione da HIV, e in particolare la condizione di un severo deficit immunologico, rappresenta un fattore di rischio correlato ad una maggiore incidenza di meningiti da Gram-negativi, rispetto alla popolazione generale. In uno studio retrospettivo di coorte su pazienti adulti con diagnosi di meningite da Gram-negativi ricoverati tra il 2007 e il 2009 a Soweto, 19 (73%) erano HIV-Ab positivi, con mediana di linfociti CD4+ 24/ml (3).
Descriviamo qui il caso clinico di un paziente di sesso maschile, di 55 anni, di origine bosniaca, in Italia da circa 30 anni, seguito presso la Divisione di Malattie Infettive dell'ospedale S. Chiara di Trento per infezione da HIV.

Sieropositivo noto dal luglio 2020 con diagnosi di AIDS per *wasting syndrome*, infezione disseminata da citomegalovirus, encefalopatia HIV-correlata, e abuso alcolico cronico. La tipizzazione linfocitaria documentava una conta di linfociti T CD4+ pari a 20/mL (2,8%) con HIV-RNA di 461.000 copie/ml. Venivano avviate terapia antiretrovirale con abacavir/lamivudina/dolutegravir e antivirale con valganciclovir e profilassi primaria con cotrimossazolo. Ai controlli successivi il paziente si presentava in buone condizioni generali e si osservava un progressivo miglioramento dell'assetto immuno-virologico con soppressione virologica (HIV RNA<20 copie/ml) e graduale recupero dei linfociti CD4+ (linfociti TCD4+ 140/mL; 9.8%). Nell'aprile 2022 la terapia antiretrovirale veniva semplificata a lamivudina/dolutegravir e veniva sospesa la profilassi primaria con cotrimossazolo. L'ultimo controllo immuno-virologico del giugno 2023 documentava un valore di linfociti T CD4+ pari a 208/mL (11%) con HIV-RNA<20 copie/ml. In data 12/10/23 accedeva in pronto soccorso per febbre, cefalea, vomito e diarrea riferiti essere presenti da circa quattro giorni. Gli esami ematochimici evidenziavano proteina C reattiva 93 mg/dL, anemia macrocitica, glicemia 125 mg/dL, globuli bianchi nella norma e tampone nasofaringeo per SARS-CoV2 negativo. La tomografia assiale computerizzata dell'encefalo e la radiografia del torace erano negativi. Effettuava emocolture e si concordava il rientro al domicilio con valutazione il giorno dopo per ripetere controlli bioumorali.

Per il persistere di cefalea e febbre, modica rigidità nucale in data 13/10/2023 si decideva di ricoverare il paziente per gli accertamenti del caso.

All'ingresso in reparto il paziente si presentava lucido, collaborante, orientato S/T e sul sé; permaneva febbre, cefalea frontale, non fotofobia; modica rigidità nucale, non altri segni neurologici. Si ripetevano emocolture su puntata febbrile.

Si decideva pertanto di effettuare rachicentesi diagnostica. Il liquor risultava limpido, incolore con, al citobiochimico, 256 polimorfonucleati/mm3, iperprotidorrachia (184 mg/dL) e ipoglicorrachia (6 mg/dL).

L' esame microbiologico identificava, alla colorazione di Gram, presenza di bastoncini Gram-negativi. In empirico veniva avviata terapia antibiotica con meropenem. Il film array risultava positivo per E.coli senza evidenza di geni di resistenza.

Il giorno 14/10 veniva comunicata dalla microbiologia la tipizzazione completa che confermava la presenza a livello liquorale di Escherichia coli toti-sensibile. Nei giorni successivi veniva comunicato dalla microbiologia la positività di tutte le emocolture eseguite all'ingresso (6/6) per Escherichia coli, con pattern di sensibilità analogo a quello isolato su liquor.

In data 16/10/2023 la terapia antibiotica veniva pertanto semplificata a ceftriaxone (2 gr per due al dì per via endovenosa). Una valutazione neurologica effettata per il persistere di iperpiressia consigliava di proseguire quanto in atto. A completamento diagnostico il paziente eseguiva RMN encefalo che confermava il noto quadro di encefalopatia HIV-correlata, con ampliamento del sistema ventricolare sovratentoriale.

Il quadro neurologico migliorava progressivamente nei giorni successivi, con risoluzione della cefalea e normalizzazione della curva termica. Venivano ripetute emocolture di sorveglianza che risultavano negative. Le sierologie per virus epatici, Quantiferon, Borrelia, Lue, TBE (tick born encephalitis) risultavano negative mentre la sierologia per Toxoplasma gondii era indicativa di infezione pregressa. Coprocolture ed esame parassitologico erano negativi così come la ricerca della tossina del Clostridium difficile.

Durante la degenza proseguiva la terapia antiretrovirale e al controllo dell'assetto immuno-virologico si evidenziavano un valore dei linfociti T CD4+ pari a 149/mL (14%) ed HIV RNA plasmatico <20 copie/mL. Dato il riscontro di valori pressori borderline, veniva valutato dall'internista che poneva indicazione all'avvio di terapia antiipertensiva con ramipril 10 mg/die.

Per il persistere di diarrea con feci liquide, presente già da qualche settimana e l'evidenza di progressiva anemizzazione con valori di Hb<11 g/dL, oltre alle indagini microbiologiche su feci, si sottoponeva il paziente ad ulteriori accertamenti che documentavano la presenza di sangue nelle feci (due campioni su tre di sangue occulto risultavano positivi) e ipovitaminosi B e iposideremia. Veniva quindi programmata colonscopia che evidenziava la presenza di lesione vegetante e ulcerata del retto inferiore e medio; l'esame istologico poneva diagnosi di adenoma tubulo-villoso del grosso intestino con displasia di alto grado e adenocarcinoma in situ e infiltrante, moderatamente differenziato, con intensa reazione desmoplastica.

Effettuava TC stadiazione oncologica per definire

l'iter terapeutico; confermata la nota lesione a livello del retto medio e inferiore con estensione longitudinale di circa 8 cm con linfoadenopatia satellite, non escluso coinvolgimento del margine anale.
Come reperto accessorio, si evidenziava trombosi della vena ascellare di destra; il reperto veniva confermato da Eco-colordoppler venoso; veniva quindi impostata terapia anticoagulante con enoxaparina, con stretto monitoraggio clinico e laboratoristico.
In data 03/11/2023 dopo tre settimane totali di terapia antibiotica, si sospendeva ceftriaxone. Il paziente si presentava in buone condizioni generali; stabilmente apiretico; completamente risolta la cefalea. Gli ematochimici documentavano GB 4500/ml, Hb 11,2 g/dL, PCR 4 mg/L.
Il paziente veniva dimesso, in attesa di discussione multidisciplinare del caso clinico dall'equipe chirurgica e oncologica.

Come descritto nella letteratura, la maggior parte dei pazienti con diagnosi di meningite da germi Gram-negativi presenta una o più co-morbidità considerate fattori di rischio (4).
Il paziente descritto nel caso clinico presentava plurimi fattori di rischio: infezione da HIV, abuso di alcolici e il riscontro durante la degenza di lesione ulcerata al retto.
In particolare, il quadro immuno-virologico alla diagnosi di infezione da HIV era estremamente compromesso, nonostante l'avvio della HAART abbia documentato la soppressione virologica con un discreto recupero del numero dei linfociti CD4+.
In merito all'eziologia da E.coli, inoltre, ricordiamo come il tratto gastrointestinale e urinario siano potenziali fonte di batteriemie e come la traslocazione di tale germe possa avvenire per la proliferazione a livello dell'intestino o dopo procedure chirurgiche. ■

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Tra i pazienti con dati virologici disponibili, il 98,6% (IC 95% [97,0%-99,5%], 426/432) ha mantenuto l'HIV-1 RNA <50 copie/mL alla settimana 240 (missing = excluded); quando i dati virologici mancanti sono stati considerati un fallimento, il 67,2% (IC 95% [63,4%-70,8%], 426/634) ha mantenuto l'HIV-1 RNA <50 copie/mL.[1] Non è stata rilevata alcuna resistenza emergente al trattamento con BIKTARVY®. Eventi avversi farmaco correlati hanno portato all'interruzione del trattamento in una percentuale <1% dei partecipanti (n=5/634).[1]

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