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Sitges, 27-30 de noviembre de 2022

Sesión Póster Oral 1 – Pósteres Orales
Comorbilidades – 28 de noviembre – 15:00-16:45h

PO-01. PROYECTO PERFILES, CLASIFICACIÓN DE PVVIH SEGÚN COMORBILIDADES E ÍNDICE CHARLSON

M. Riera[1], F.J. Fanjul[1], F. Homar[2], A. Villoslada[2], A. Rey Ferrin[3], L. Villaplana[4], F. Artigues[1], P. Sorni[2], J. Serra[3], L. Ventayol[4], M. Peñaranda[1] y J. Murillas[1]

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Introducción: En el año 2020 se inició el Proyecto PERFILES cuyos objetivos son: 1. Implementar un gestor clínico común (eVIHa) para la asistencia de los pacientes con infección VIH (PVVIH) en las Islas Baleares capaz de estratificar y monitorizar los cuidados recibidos por los pacientes. 2. Definir perfiles de PVVIH en función de sus necesidades asistenciales. 3. Estratificar los pacientes de la cohorte eVIHa Balear mediante los perfiles definidos e implementar circuitos asistenciales para cada perfil.
Métodos: Población: PVVIH en seguimiento en las Unidades de VIH de las Islas Baleares. Se clasificó a los pacientes según tres perfiles en función de sus necesidades asistenciales; 1) Perfil VIH-pluripatológico: pacientes que presentaban 3 o más ENOS crónicos o un índice de Charlson igual o superior a 4 (considerando SIDA igual a 1). 2) Perfil psiquiátrico VIH: pacientes que presentaban patología psiquiátrica grave en tratamiento, incluyendo síndrome de dependencia crónica al alcohol. 3): Perfil de bajo riesgo: pacientes que no cumplían criterios de ninguno de los perfiles previos. Según tratamiento crónico obtenido de la tarjeta sanitaria y datos de laboratorio se sugiere al facultativo inclusión en determinadas patologías crónicas.
Resultados: Se incluyeron 3.537 pacientes atendidos en los hospitales de Mallorca (2.090 de HUSE, 1.001 de HUSE, 204 HCIN y 231 HMAN). De ellos 801 son mujeres (22,7%) y 2.735 hombres (77,7%), siendo la edad media de 49,9 años (DE 11,3). Por lugar de procedencia 2.860 (80,8%) son europeos, 533 (15,1%) de Sudamérica, y 128 (3,3%) de África. Por grupo de riesgo se incluyeron como HSH 1.492 (42,2%), HTSX (31,6%), IDU 711 (21,1%), UK 763 (4,5%). Por estadio de CDC se consideraron estadio A, 2.255 pacientes (63,9%), B 491 (13,9%) y C 768 (21,7%). Al evaluar el perfil de cronicidad, 350 pacientes (9,9%) se incluyeron en el perfil de VIH-Pluripatológico, 132 presentaban puntuación de I. Charlson ≥ 4 y 320 presentaban 3 o más comorbilidades/ENOS. Se clasificaron como perfil psiquiátrico 186 pacientes (5,3%) de los que 166 presentaban una patología psiquiátrica grave y 20, 2 o más. Los restantes 3.087 pacientes (87.3%) se consideraron perfil de bajo riesgo.
Conclusiones: La implementación de una herramienta de gestión clínica común permitió una estratificar eficazmente a los PVVIH en perfiles predefinidos en función de antecedentes médicos y necesidades asistenciales.

PO-02. HERRAMIENTAS DE ESTRATIFICACIÓN DE PACIENTES. APLICACIÓN EN UNA COHORTE DE PERSONAS QUE VIVEN CON VIH SEGUIDAS EN UNA UNIDAD DE REFERENCIA

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Objetivos: Estratificar y calcular la complejidad de una cohorte de personas que viven con VIH (PVV). Calcular los tiempos de atención en consulta no urgente para cada perfil para proponer mejoras en la atención de PVV.
Métodos: Estudio realizado en una cohorte de 1.424 PVV en seguimiento que representa un área sanitaria de 549.000 habitantes. Para la estratificación y cálculo de complejidad se ha utilizado la herramienta de GESIDA, incorporada en SIMON (sistema inteligente de monitorización), que es el gestor de seguimiento en uso en la unidad. Se ha recogido el tiempo utilizado para la asistencia en consulta no urgente durante 12 meses (sept-21 a ago-22) mediante el aplicativo Chronos. Se registraron las ausencias a consulta, y el número de atenciones (tanto urgentes como no) de cada perfil en el periodo de estudio.
Resultados: De las 1.310 PVV incluidas en SIMON, se han estratificado 945 (72,1%): edad 43 ± 11 años, 77,5% varones, 69,9% blancos europeos, 28,4% categoría C-CDC, con 16 años (10-26) de infección VIH. El 95% tiene ARN-VIH < 200 cop/mL con 692 ± 365 CD4/µl. Complejidad: baja (39,4%), media (20,3%), alta (19,0%), extrema (21,3%). Estratificación, perfiles: 35,0% azul, 11,5% amarillo, 8,7% morado, 12,3% verde, 0,2% fucsia, 11,2% lila, 4,4% naranja y 15,7% no clasificable (la mayoría corresponden a perfil amarillo con problemática social o con conductas sexuales de riesgo, de ellos el 70,8% tienen complejidad extrema). Tiempo medio en consulta no urgente y media de consultas no urgentes/año: azul 13 ± 7 minutos, 2,6 ± 1,4 consultas/año; amarillo 29 ± 14 minutos, 3,3 ± 1,5 consultas/año; morado 26 ± 16 minutos, 2,9 ± 2,0 consultas/año; verde 19 ± 12 minutos, 2,8 ± 1,9 consultas/año; lila 21 ± 11 minutos, 2,3 ± 1,2 consultas/año. El 20,4% de las consultas no urgentes se realizaron telemáticamente, con más

frecuencia en el perfil azul (24,8%). El perfil verde presentó más ausencias en consulta (18%) seguido del morado (14%). El perfil amarillo perfil lila requirió más consultas urgentes (3 ± 2 consultas/año), seguido del amarillo (2 ± 1 consultas/año).

Conclusiones: Las herramientas de estratificación son útiles para mejorar la organización de las consultas en las Unidades de seguimiento. La herramienta no clasifica a 1/6 de las PVV. Una asignación de tiempo en consulta no urgente igual a todas las PVV (15 minutos) no parece eficiente. Las PVV de perfil amarillo requieren el doble de tiempo en consulta que el perfil azul. La estratificación puede ayudar a individualizar y optimizar los tiempos de asistencia en consulta con una mejora en la calidad asistencial y en la satisfacción de usuarios y profesionales sanitarios.

PO-03. HEALTH-RELATED QUALITY OF LIFE IN PEOPLE LIVING WITH HIV FROM THE MULTICENTER COHORT OF THE SPANISH AIDS RESEARCH NETWORK (CORIS-QOL)

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Introduction: We aimed to describe health-related quality of life (HRQoL), describe general HRQoL and its different dimensions, and its clinical and sociodemographic determinants in people living with HIV (PWH) from the cohort of the Spanish AIDS Research Network (CoRIS).

Methods: We designed a mobile app to routinely collect, every 3 months, data on HRQoL among individuals in active follow-up in CoRIS from July 1, 2021; recruitment is still on-going. HRQoL was measured through the self-reported WHOQoL-HIV-Bref questionnaire, comprising 31 items: 1 on global HRQoL, 1 on general health and 29 covering 6 domains: physical health, psychological health, level of independence, social relationships, environmental health, and spirituality, religion and personal beliefs (SRPB). We calculated means and 95% confidence intervals (95%CI) for each item (rated 1-5) and domain (rated 4-20); higher scores denote higher quality of life. We used multivariable logistic regression models to calculate Odds Ratios (OR) for the association between sociodemographic and clinical characteristics with good/very good global HRQoL.

Results: By August 25, 2022, 181 individuals from 18 centers answered the baseline questionnaire: 91.7% were men, median age was 44 (IQR: 36-51) years, 67.6% were from Spain and 85.2% acquired HIV through sex between men. Median time from HIV diagnosis was 7 (IQR: 4-11) years, 99.3% were receiving antiretroviral treatment (ART) (most receiving BIC/FTC/TAF [30.5%], DTG/3TC [20.6%] and DTG/3TC/ABC [9.9%]), and 95.0% were virally suppressed. The figure shows mean scores of each item and domain. The items showing the lowest scores were sexual satisfaction, forgiveness and blame, and sleep and rest, while mobility and symptoms of HIV presented the highest scores. Across domains, level of independence and physical and environmental health showed the highest scores while SRPB showed the lowest score. 52.5% of individuals reported good/very good HRQoL. Living with HIV for less than 2 years (adjusted OR: 0.32; 95%CI: 0.09-1.08) and having had an AIDS diagnosis (0.25; 0.06-1.04) were associated with a lower chance, borderline significant, of good/very HRQoL.

Conclusions: In this cohort of PWH, mostly men receiving ART and virally suppressed, only half of the participants reported a good HRQoL. HRQoL was lower among recently diagnosed individuals and those who had had AIDS. Sexual satisfaction, forgiveness and blame, and sleep and rest, showed the lowest HRQoL scores.

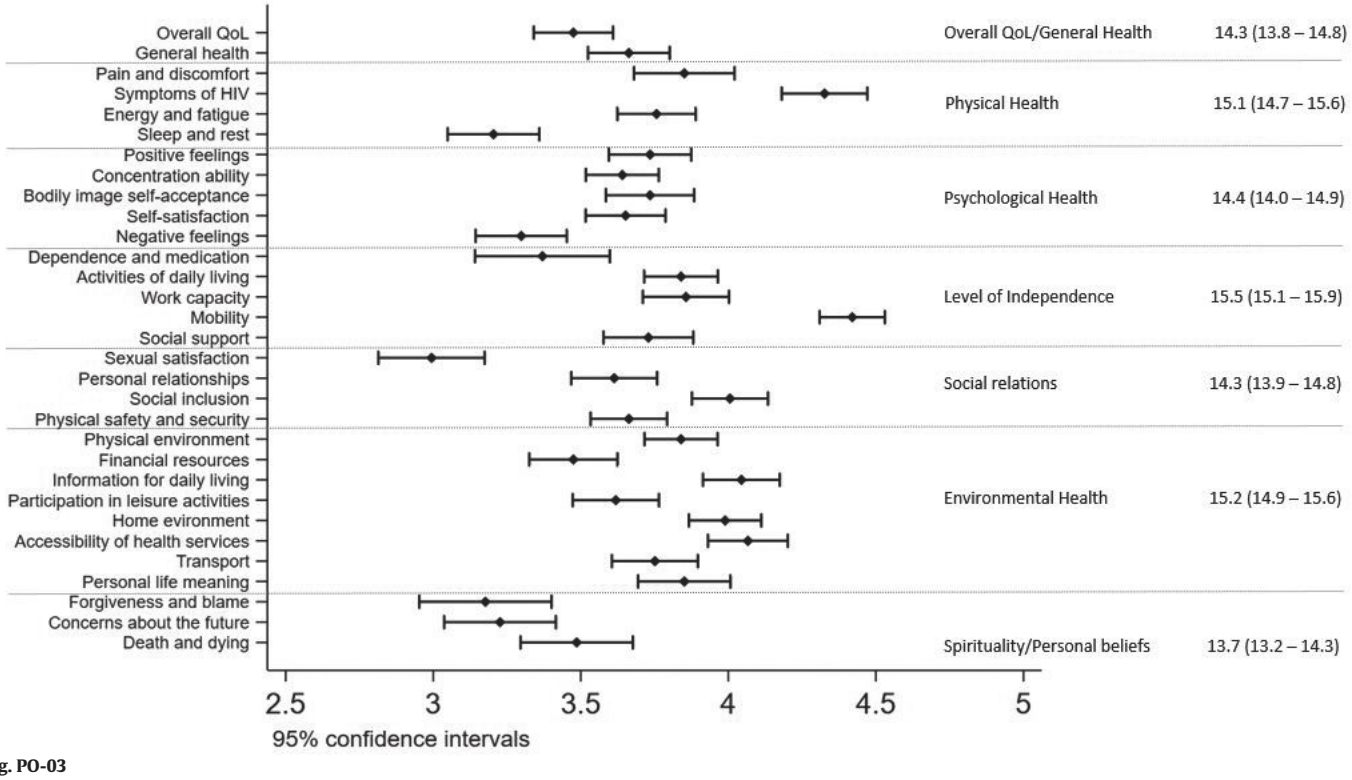

Fig. PO-03

PO-04. IMPACTO DEL ESTADIO DE ENFERMEDAD HEPÁTICA SOBRE EL MICROBIOMA SANGUÍNEO Y SU INTERRELACIÓN CON EL METABOLOMA EN PACIENTES CIRRÓTICOS POR VHC CON Y SIN VIH

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Introducción: La cirrosis es una complicación de la infección por el virus de la hepatitis C (VHC) y un factor de riesgo para el desarrollo de insuficiencia hepática y carcinoma hepatocelular. En pacientes con cirrosis, la translocación bacteriana intestinal contribuye al desarrollo de complicaciones hepáticas y mortalidad. El riesgo de estas complicaciones puede ser estimado mediante el índice de Child-Turcotte-Pugh (CTP). Nuestros objetivos han sido el estudio de la asociación entre los valores de CTP y el microbioma sanguíneo y el análisis del perfil metabolómico en pacientes con cirrosis por VHC.

Métodos: Se realizó un estudio multicéntrico transversal en 88 pacientes con cirrosis por VHC (61 coinfectados por el VIH) con valores de CTp < 7 (enfermedad compensada) y CTP ≥ 7 (compromiso funcional significativo o descompensación). Se analizó el microbioma sanguíneo mediante amplificación y posterior secuenciación de las regiones V3-V4 del ADN ribosómico 16S bacteriano. Se estudiaron las diferencias en α-diversidad, β-diversidad y abundancia relativa de unidades taxonómicas operativas (OTUs) entre pacientes con CTp < 7 y pacientes con CTP ≥ 7 mediante modelos lineales generalizados multivariantes (ALDEx2). Además, se llevó a cabo un análisis de correlación entre los taxones significativos y el perfil metabolómico en plasma, determinado mediante cromatografía de gases y cromatografía de líquidos con ionización positiva y negativa.

Resultados: No se observaron diferencias significativas entre grupos (CTp < 7 vs. CTP ≥ 7) para las variables clínicas y epidemiológicas más relevantes. Los pacientes con CTP ≥ 7 mostraron un microbioma sanguíneo con: a) menor α-diversidad para filo (Chao1: ratio de la media aritmética ajustada (aAMR) = 0,85 (0,74-0,97), p = 0,021; Shannon: aAMR = 0,80 (0,69-0,93), p = 0,005; y Simpson: aAMR = 0,94 (0,87-1,03), p = 0,006) y clase (Chao1: aAMR = 0,85 (0,74-0,97), p = 0,019) con respecto a pacientes con CTp < 7; b) menor β-diversidad, para clase y orden (p = 0,010 y p = 0,018); c) diferencias en abundancias relativas de OTUs, con enriquecimiento significativo del phylum *Proteobacteria*, la clase *Alphaproteobacteria* y el orden *Sphingomonadales* (*fold change* (FC) = 1,53, p = 0,120; FC = 1,57, p = 0,016; y FC = 1,52, p = 0,050, respectivamente). Cuando se analizó la correlación entre estos taxones y el perfil metabolómico, se encontraron correlaciones positivas entre *Proteobacteria* y etanolamina y ácido oleico en cromatografía de gases y correlación negativa para *Proteobacteria* y *Sphingomonadales* con p-Cresol en cromatografía de gases y líquidos.

Conclusiones: Los pacientes con CTP ≥ 7 presentaron una menor diversidad del microbioma sanguíneo, así como una mayor abundancia relativa del phylum *Proteobacteria*, la clase *Alphaproteobacteria* y el orden *Sphingomonadales*. Además, esta disbiosis sanguínea correlacionó con los niveles de ciertos metabolitos plasmáticos. Se necesita de más estudios para esclarecer la implicación biológica de estos hallazgos.

PO-05. GENETIC CONTRIBUTION TO WEIGHT GAIN AFTER INITIATION OF ANTIRETROVIRAL THERAPY IN TREATMENT *NAÏVE* PATIENTS WITH HIV

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Introduction: We studied the association of obesity-related single nucleotide polymorphisms (SNPs) with weight gain after antiretroviral therapy (ART) in people with HIV (PWH).

Methods: Participants were ART-*naïve* PWH, recruited in the Spanish HIV Research Cohort (CoRIS), who started ART from 2014 onwards, had weight and height information at baseline and 96 weeks from the beginning of ART, and had blood/DNA deposited in the CoRIS Biobank. The primary outcome variable was a change in weight at 96 weeks after starting ART. We genotyped 14 obesity-related SNPs from a meta-analysis of genome-wide association studies (GWAS) body mass index (BMI) loci (Nature. 2015;518:197-206). Changes over time in weight and BMI were studied using adjusted linear mixed models for longitudinal data (LMM), considering SNPs, time, and their interaction as fixed effects and the patient as a random effect.

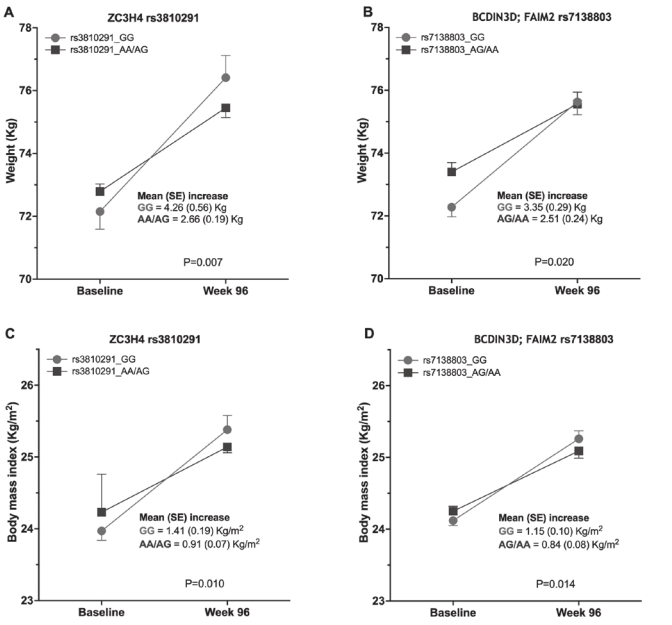

Figure. Reuslts of linear mixed models adjusted by age, sex, country of birth, prior AIDS-defining conditions, CD4+ cell count, HIV-RNA viral load, type of ART regimen according to anchor drug, and NRTI backbone. **ZC3H4**, Zinc Finger CCCH-Type Containing 4; **BCDIN3D**, BCDIN3 Domain Containing RNA Methyltransferase; **FAIM2**, Fas Apoptotic Inhibitory Molecule 2

Results: A total of 1,021 PWH were included. The mean weight gain over 96 weeks was 2.90 (95%CI: 2.54-3.26) Kg. Factors associated with weight gain were female sex, birth in Sub Saharan Africa, prior AIDS, CD4+ < 200 cells/uL, HIV-RNA > 100,000 copies/mL, negative HCV serology, and use of tenofovir alafenamide. By adjusted LMM, a significant association was found between *ZC3H4* rs3810291 GG genotype and *BCDIN3D/FAIM2* rs7138803 GG genotypes polymorphisms and weight and BMI increase. The estimated adjusted mean (standard error [SE]) of weight gains were 4.26 (0.56) Kg in *ZC3H4* rs3810291 GG carriers and 2.66 (0.19) Kg in AA/AG carriers (p = 0.007). Likewise, the estimated means (SE) weight gain at 96 weeks were 3.35 (0.29) Kg in *BCDIN3D/FAIM2* rs7138803 GG carriers and 2.51 (0.24) Kg in AG/AA carriers (p = 0.020) (Fig.).
Conclusions: Our findings suggest that genetic factors play a role in weight gain after ART initiation. Further work is needed to understand how ZC3H4 and BCDIN3D/FAIM2 polymorphisms lead to higher weight gain in this clinical context.

PO-06. NEW-ONSET DIABETES IN PERSONS WITH HIV ON BIC/FTC/TAF *IN REAL-WORLD CLINICAL PRACTICE*

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Introduction: The influence of new integrase strand-transfer inhibitors (INSTI)-based antiretroviral therapy (ART) on Type 2 Diabetes in people with HIV remain incompletely defined. To describe the prevalence and incidence of Prediabetes and Diabetes in a cohort of HIV people receiving BIC/FTC/TAF.
Methods: Clinic-based study in a tertiary, University Hospital in Madrid. HIV-infected individuals starting on or switching to BIC/FTC/TAF (June 2018-July 2021) were included. Data collected for sample selection included multiple fasting blood glucose and/or HBA1c measurements at first data collection date and all available values after starting treatment from BIC/FTC/TAF onwards and the date of BIC/FTC/TAF initiation. Diabetes and Prediabetes were diagnosed if they met criteria in two or more consecutive blood test according to the American Diabetes Association (ADA) definitions of Diabetes (fasting plasma glucose at or above 126 mg/dL, HBA1c > 6.5%) and Prediabetes (HBA1c of 5.7%-6.4% or fasting blood sugar of 100-125 mg/dl).
Results: The analysis focused on 1,078 (360 *naïve* and 718 switch) BIC/FTC/TAF participants with completed data, excluding 63 (8 *naïve* and 55 switch) who had previous diabetes. Of the selected 1078 patients, median age stood at 48 years, 15% were women, 65% European. Mean time follow-up in those patients without new Diabetes diagnosis during the study period was 76.7 (56-92) weeks. Globally 25 out of 1,078 (2.3%) developed new Diabetes in a mean time of 47.7 (21-78) weeks. At their first visit on BIC/FTC/TAF, 198 out of 1078 (18.4%) met previous Prediabetes criteria and in this group of patients Diabetes developed in 16/198 (8.1%) after BIC/FTC/TAF initiation. Among 880 people without Prediabetes criteria at their first visit on BIC/FTC/TAF, during follow-up Prediabetes developed in another 103 people (11.7%), mostly 62 (60.2%) ART-experienced, and new Diabetes developed in 11/880 (1.2%), six of them had switched from previous ART.
Conclusions: Diabetes was more frequent after progression from Prediabetes than new-onset Diabetes in patients on BIC/FTC/TAF. Most patient with Prediabetes or Diabetes diagnosis after BIC/FTC/TAF initiation were ART-experienced. Information about previous Prediabetes could be important to address the potential impact of each INSTI regimen influence on the onset of Diabetes.

PO-07. CAMBIOS METABÓLICOS DE LA SIMPLIFICACIÓN A BICTEGRAVIR/EMTRICITABINA/TENOFOVIR ALAFENAMIDA DESDE REGÍMENES SIN TENOFOVIR DIFUMARATO NI TENOFOVIR ALAFENAMIDA. ESTUDIO METABIC

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Introducción: El cambio de regímenes que incluyen tenofovir difumarato (TDF) a bictegravir/emtricitabina/tenofovir alafenamida (B/F/TAF) se ha asociado con aumento de peso, peor perfil lipídico y esteatosis hepática. El objetivo de este estudio es evaluar los cambios metabólicos a los 6 meses y al año tras el cambio de regímenes que no incluyan TDF ni TAF a B/F/TAF.
Métodos: Estudio de cohortes retrospectivo de PVV que simplificaron a un régimen de B/F/TAF desde regímenes sin TDF ni TAF entre enero 2019 y mayo 2022 con un seguimiento mínimo de 6 meses. Objetivo primario: cambio absoluto de las fracciones lipídicas a los 6 meses. Objetivos secundarios: cambio de las fracciones lipídicas a los 12 meses y cambio en la glucosa, creatinina y cociente triglicéridos/glucosa (TyG) para esteatosis hepática (EH) y resistencia a la insulina (RI) a los 6 meses y a los 12 meses. Se utilizaron modelos lineales generalizados.
Resultados: Se incluyeron 147 PVV, 81% varones con una mediana (P25-75) de edad 55 años (46-58), células CD4+ 675 cels/mm^3 (449-879) y 79.6% con carga viral < 50 cp/ml. Al inicio 44 (30%) tenían hipertensión, 72 (49%) dislipemia, 24 (16%) diabetes, and 46% obesidad o sobrepeso. La mayoría de los participantes (97; 66%) provenían de triple terapia con inhibidor de la integrasa (ABC/3TC + dolutegravir o raltegravir), y 28 (19%) de un inhibidor de la proteasa potenciado (9 3TC+IP, 10 monoterapia IP). A los 6 meses hubo una reducción significativa del colesterol total –9,45 mg/dl (IC95% –16,43 –2,48; p = 0,004), y del cociente TyG-EH de –0,147 (IC95% –0,25, –0,04; p = 0,0023). El porcentaje de pacientes con EH por TyG al inicio, 6 y 12 meses fue 75, 65, y 72. El porcentaje de pacientes con RI por TyG al inicio, 6 y 12 meses fue de 78, 69 y 83. Estas diferencias no fueron estadísticamente significativas. A los 6 y 12 meses hubo una reducción significativa del filtrado glomerular (CKD-EPI) –1,87 ml/min (IC95% –3,62, –0,11; p = 0,0319) y –2,73 ml/min (-4,52, –0,95; p < 0,001) respectivamente. NO hubo cambios significativos en el resto de parámetros metabólicos.
Conclusiones: En esta cohorte el cambio a B/F/TAF de regímenes sin TDF ni TAF mejora el colesterol total a los 6 y 12 meses y es neutral para resto de parámetros metabólicos.

PO-08. METABOLIC-RELATED OUTCOMES AFTER SWITCHING FROM TENOFOVIR DISOPROXIL FUMARATE TO TENOFOVIR ALAFENAMIDE IN ADULTS LIVING WITH HIV: A MULTICENTER PROSPECTIVE COHORT STUDY

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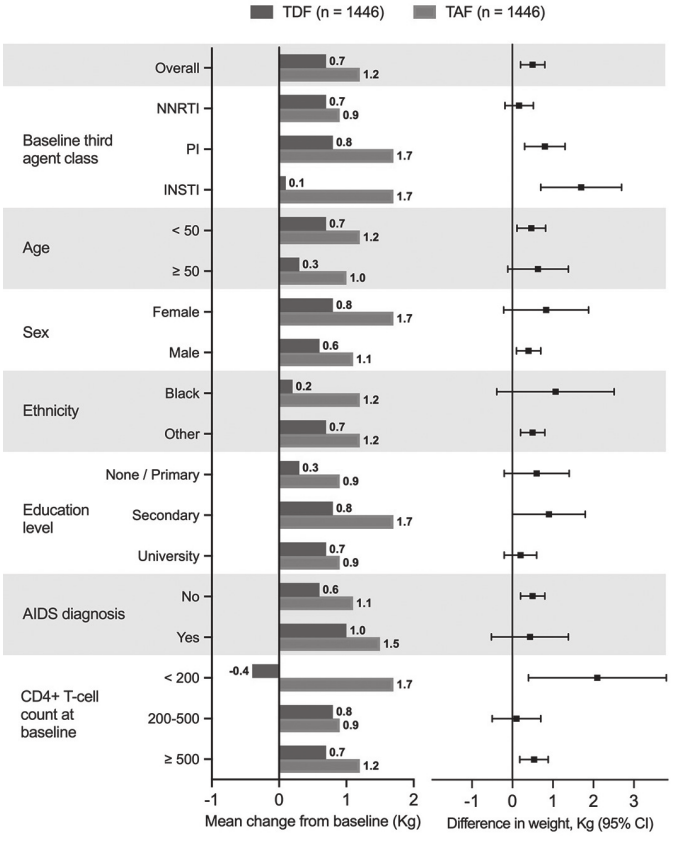
Introduction: Tenofovir alafenamide (TAF) is widely used to avoid the bone and kidney toxicity associated with tenofovir disoproxil fumarate (TDF). However, concerns remain about potential metabolic

complications of TAF. We aimed to evaluate changes in weight, laboratory markers, and metabolic-related clinical events after replacing TDF with TAF.

Methods: Multicenter prospective cohort study in the Spanish CoRIS cohort. We included virologically suppressed adults with HIV receiving TDF for more than 12 months who either switched to TAF or maintained TDF, with no changes in the core agent. Participants were matched by propensity score. We fitted generalized equation models to assess changes in weight, blood lipids, and hepatic steatosis index, and to compare the incidence of diabetes, hypertension, and lipid-lowering drug use after 144 weeks.

Results: 1,446 participants were matched in each group. Median age was 38 years, 85% were male, mean weight at baseline was 73 kilograms. Participants who switched to TAF had a mean weight increase of +0.5 kg (95%CI 0.2-0.8, p = 0.001) at 144 weeks over those who maintained TDF (Figure), with no difference in the occurrence of overweight or obesity. Between-group weight differences of TAF compared with TDF were larger among participants receiving INSTI, women, black ethnicity, and those with CD4+ < 200 cells/µL. Participants who switched to TAF had a significantly higher increase in total cholesterol (+7.9 mg/dL), low-density lipoprotein (LDL)-cholesterol (+4.1 mg/dL), high-density lipoprotein (HDL)-cholesterol (+1.7 mg/dL), and triglycerides (+11.2 mg/dL) at 144 weeks. There were no differences in total cholesterol-HDL ratio or hepatic steatosis index. During follow-up, 20 individuals (1.4%) who switched to TAF were diagnosed with new-onset diabetes, 51 (3.5%) with hypertension, 76 (5.2%) started a new lipid-lowering agent, and 76 (5.2%) met NAFLD criteria. No significant differences were observed with participants who continued on TDF, of whom 1.4% developed diabetes, 4.8% developed hypertension, 4.4% used a new lipid-lowering agent, and 5.8% met NAFLD criteria (all p > 0.100).



Conclusions: Switching from TDF to TAF was associated with a 0.5 kg weight gain over 144 weeks with no difference in overweight or obesity or metabolic clinical events. LDL, HDL, and triglycerides increased with no difference in total cholesterol-HDL ratio.

PO-09. EFFECTS OF AN ONLINE-BASED COGNITIVE STIMULATION TRAINING AS A PREVENTIVE PROGRAM IN PATIENTS WITH HIV: A PROOF OF CONCEPT STUDY

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Introduction: Cognitive complains, frequently detected among people living with HIV (PLH), could be associated with interferences on daily living due executive dysfunction that impact their quality of life.

Methods: Our proof of concept study was to design and evaluate the feasibility and acceptability of an online cognitive stimulation program (OCSP) as an adjuvant therapy for PLH complaining of cognitive-disturbances. The OCSP entails 24 sessions distributed in 12 weeks with 40minutes of self-applied exercises, specifically shaped on affected cognitive domains in PLH. Feasibility and acceptability were assessed using specific self-reported questionnaires (indicated in table) and a satisfaction and utility visual analog feedback survey (VAS)] focused on determinants of brain health and key health outcomes, applied before and after the OCSP.

Results: Current analysis included the first 36 participants who started OCSP. Thein participants were primarily men (86%) in their 60s (mean-age: 60.5 ± 7), with > 8 years of school education (86%). Around 40% were currently employed and 37% were retired. Mean global deficit score (GDS) at baseline was 0.6 (mean GDS: 0.6 ± 0.5). The 81% of participants completed all the sessions and the 19% left remain 1-2 sessions to complete. Numerically we observed changes reducing 33.2% of functional cognitive complains (PAOFI) and 9.4% of dysexecutive complains (Table). Furthermore, we observed a significant reduction in self-reported anxiety levels (HADS-anxiety raw results), though depressive symptoms (HADS-depression scale) remained the same. The feedback of the participants indicated high grades of satisfaction, perceived value and interest in the program.

Participants self-reported perception before and after completing the OCSP

Questionnaire	Baseline	After	Change	p
PAOFI				
M (SD)	4.72 (7.19)	4.61 (7.03)	-0.11 (1.68)	0.87
score > 3, (n%)	9 (25.0)	6 (16.7)	-33.2%	0.375[a]
DEX Total				
M (SD)	22.75 (12.727)	20 (11.17)	– 2,75 (2.82)	0.12
score > 9, (n%)	32 (88.9)	29 (80.5)	-9,40%	0.161
DEX disorganization/apathy				
M (SD)	12.36 (7.60)	11.14 (7.57)	-1.22 (1.79)	0.21
score > 9, (n%)	23 (63.95)	20 (55.6)	-13,10%	0.46
DEX disinhibition/impulsivity				
M (SD)	10.39 (5.78)	8.86 (5.1)	-1.53 (1.29)	0.12
score > 9, (n%)	18 (50.0)	16 (44.4)	-11.2%	0.774
HADS-Anxiety				
M (SD)	8.75 (3.99)	7.55 (3.86)	-1.2 (0.92)	0.03
score > 7, (n%)	20 (55.56)	15 (44.44)	-20%	0.17
HADS-Depression				
M (SD)	5.97 (4.19)	5.36 (4.21)	-0.61 (0.99)	0.26
score > 7, (n%)	26 (72.2)	26 (72.2)	0%	1.000[a]
Satisfaction degree VAS		8.42 (1.91)		
Invested time VAS		8.61 (1.87)		
Utility perceived VAS		8.33 (2.13)		

OCSP: Online Cognitive Stimulation Program; PAOFI: Patient's Assessment of Own Functioning Inventory; DEX: Dysexecutive questionnaire; HADS: Hospital Anxiety and Depression Scale; VAS: Visual Analog Scale; 0-10 , 0-worse,10-best; M (SD) Raw score, mean (SD). N (%) Functional impairment, (score > X) n%.

Conclusions: Our findings support the feasibility and acceptability of our OCSP. A larger sample size is needed to confirm the potential

benefits observed on functional cognitive complains, dysexecutive disability and anxiety and the effectiveness of online cognitive stimulation programs.

PO-10. EVOLUCIÓN DE LOS NIÑOS CON DIAGNÓSTICO DE INFECCIÓN VIH EN 2018 DE LA RED PLANTAIDS DURANTE LA PANDEMIA COVID

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Introducción y objetivos: A pesar de que la tasa de transmisión materno-infantil (TMI) del VIH en Latinoamérica se ha reducido considerablemente, la población pediátrica constituye uno de los grupos más vulnerables en esta región. El objetivo principal del estudio es describir la situación clínica, analítica y psicosocial de los nuevos diagnósticos de VIH de TMI en 2018 tres años después. Como objetivos secundarios se plantea evaluar la relación entre el diagnóstico precoz (menos de 1 año) y la adherencia terapéutica en la evolución de los pacientes, y describir la frecuencia y características de la infección aguda por SARS-CoV-2.
Métodos: Se recogen variables (tratamiento, estadio clínico e inmunológico, infección por SARS-CoV-2 y mortalidad) en relación al seguimiento hasta la actualidad de los nuevos diagnósticos VIH de TMI en 2018 en 10 hospitales de 8 países de Latinoamérica pertenecientes a la red PLANTAIDS.
Resultados: 72 pacientes pediátricos. Situación al diagnóstico: mediana de edad 2,55 años, 38,88% varones, 49,28% estadio clínico C, 12 pacientes < 15% CD4. Todos los pacientes iniciaron tratamiento antirretroviral (TAR) de manera inmediata (< 1 mes del diagnóstico), exceptuando un caso en el que se demoró su inicio por motivos sociales. El 57% recibió profilaxis con cotrimoxazol y el 38,10% padeció una infección oportunista (tuberculosis 33,33%). Se consiguió una cobertura vacunal adecuada, según el calendario de inmunización infantil, en el 54,1%. El 28% y el 51% de los niños menores de 5 años presentaban en la primera revisión un percentil de peso y talla menor de 3, respectivamente. Se consiguió una correcta adherencia terapéutica en el 84% de los pacientes, encontrando diferencias estadísticamente significativas en el número de infecciones oportunistas entre los niños con una adecuada adherencia y los que no (OR 0,1 [0,03-0,3], p < 0,01). No se encontraron diferencias estadísticamente significativas respecto a las características clínicas e inmunológicas y el diagnóstico precoz. Hubo tres casos de infección aguda por SARS-CoV-2, asintomáticos o sintomáticos leves. 11 pacientes perdieron el seguimiento. Cuatro pacientes fallecieron debido a infecciones oportunistas y/o estado avanzado de la enfermedad VIH.
Conclusiones: En nuestro estudio, el 98,6% de los pacientes inició TAR de manera precoz. Una mejor adherencia terapéutica disminuye el riesgo de infecciones oportunistas. La infección VIH diagnosticada en la edad pediátrica tiene un mal pronóstico. La infección SARS-CoV-2 en niños con VIH no parece cursar de forma grave.

Sesión Póster Oral 2 – Pósteres Orales Básicos – 28 de noviembre – 15:00-16:45h

PO-11. EPIDEMIOLOGÍA MOLECULAR DEL SUBSUBTIPO A6 DEL VIH-1 EN ESPAÑA

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Introducción y objetivos: El subsubtipo A6 del VIH-1 predomina en la mayoría de los países de la antigua Unión Soviética (AUS). Dicha variante se ha asociado a fracaso terapéutico con tratamiento con cabotegravir + rilpivirina. Aquí analizamos la presencia y transmisión de virus de subsubtipo A6 en España.
Métodos: A partir de ARN de plasma o ADN de sangre de pacientes atendidos en centros clínicos españoles de 13 CC.AA., se amplificó proteasa-transcriptasa inversa (PR-TI) mediante (RT-)PCR/PCR anidada, con posterior secuenciación. La forma genética se determinó mediante filogenia. Para identificar *clusters*, se incluyeron todas las secuencias A6 en PR-TI de la HIV Sequence Database, con análisis filogenético con IQ-Tree. Los *clusters* se definieron como aquellos con apoyo de *ultrafast bootstrap* ≥ 0,9.
Resultados: De los 13.664 individuos cuyas muestras fueron secuenciadas en PR-TI por nosotros, 78 portaban virus A6, 54% de los cuales fueron diagnosticados en los últimos 6 años. El origen de los pacientes fue un país de la AUS en 52% (la gran mayoría de Rusia o Ucrania), España en 31% y Latinoamérica en 10%. La transmisión fue heterosexual en 43%, hombres que tienen sexo con hombres (HSH) en 24%, personas que se inyectan drogas en 16% (todos de la AUS) y sexual no especificada en 10%. Entre los españoles, HSH era la categoría más prevalente (40%). Cinco españoles y 4 latinoamericanos agrupaban con otros individuos residentes en España en 3 pares y 2 tripletes. Dos de los pares incluían un individuo ucraniano, en uno de ellos con residencia en la misma ciudad. Los 2 tripletes estaban compuestos, respectivamente, por 3 latinoamericanos residentes en la misma ciudad y 3 españoles residentes en 2 provincias adyacentes. En otros países europeos se detectaron 3 *clusters* de virus A6 de ≥ 10 individuos en Alemania (n = 3) y Polonia (n = 1) y 14 *clusters* de 4 a 7 individuos en Polonia, Alemania, República Checa, Eslovenia, Hungría y Chipre.
Conclusiones: Se detectan virus del subsubtipo A6 del VIH-1 en España, mayoritariamente en pacientes de la AUS, pero también en españoles y latinoamericanos, con evidencia de transmisión local limitada. Los análisis filogenéticos sugieren probable transmisión de virus A6 en otros 6 países europeos. Estos resultados abogan por la determinación de la forma genética del VIH-1 cuando se considere tratamiento con cabotegravir + rilpivirina, con mayor motivo considerando la actual crisis migratoria provocada por el conflicto bélico en Ucrania, que previsiblemente resultará en un incremento en la difusión de virus A6 hacia la Unión Europea.

PO-12. TIGIT/CD155 AXIS BLOCKADE ENHANCES T-CELL IMMUNITY AND HIV-1-SPECIFIC DEGRANULATION IN PLWH ON ART

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Developing immune interventions is critical to attaining the HIV-1 cure. Immune checkpoint blockade has been postulated to achieve this goal. To date, these strategies focus on a relatively narrow set of targets using conventional monoclonal blocking antibodies. Although several studies have indicated the potential of targeting TIGIT immune checkpoint pathway for immunotherapeutics for people living with HIV-1 (PLWH), no focus has been paid to its ligand CD155. Here, we propose to explore CD155 as an immunotherapeutic target in PLWH. We engineered and produced two soluble Inhibitory Receptors (sIR) proteins (monomeric sIR1 and Fc-dimeric sIR2) with a sIR-Control. We determined SIRs affinity to CD155 by surface plasmon resonance and evaluated CD155 blockade in a coculture system using a Jurkat-TIGIT$^+$ reporter cell line with a BW5417:OKT3 cell line expressing CD155. Moreover, we assessed functional CD155 blockade by sIR1 and sIR2 in PBMCs of PLWH on ART (n = 17). Briefly, PBMCs were stimulated with sIR1, sIR2, and sIR-Control at 10 ug/mL in the absence or presence of an HIV-1 Gag peptide pool. After 16h, we analyzed antigen-independent and HIV-1-specific T-cell responses by flow-cytometry combining CD3, CD4, CD8, CD45RA, CCR7, CD16, CD56, CD155, TIGIT, IFNγ, TNF, CD107a, IL-2, and IL-10 markers. We determined sIR1 and sIR2 specific binding to CD155 and found an increased affinity of sIR2 (8.6 nM) compared to sIR1. In coculture experiments, only the blockade of CD155 with sIR2 increased the activation of NFkB (p = 0.043) and the coactivation of NFkB:NFAT (p = 0.0060) in Jurkat-TIGIT$^+$ reporter cells. In comparison, TIGIT blockade by mAb only increased NFkB:NFAT coactivation (p = 0.0045). Using PBMCS from PLWH, we found in an antigen-independent manner, increased production of IFNg (p = 0.0015), TNF (p = 0.0026), IL-2 (p = 0.022) and IL-10 (p = 0.0009) in CD8$^+$ T-cells and increased the production of IL-2 (p = 0.055) and IL-10 (p < 0.0001) in CD4$^+$ T-cells by sIR2. In addition, the presence of sIR2 increased the frequency of TIGIT$^+$CD8$^+$ (p < 0.0001) and TIGIT$^+$CD4$^+$ (p = 0.0017) T-cells with augmented degranulation capacity. In an antigen-dependent manner, the presence of HIV-1 gag favoured a specific increase of CD107a in TIGIT$^+$CD8$^+$ (p = 0.0033) and TIGIT$^+$CD4$^+$ (p = 0.0024) T-cells in the absence of IFNg, TNF, IL-2 and IL-10 production. No effect was found for sRI1. We generate sIR1 and sIR2 immunomodulatory proteins capable of binding CD155. Our data demonstrate significant blockade of CD155 and enhancement of T-cell cytokine production by sIR2. Moreover, sIR2 increased HIV-1-specific degranulation in TIGIT$^+$CD4$^+$ and TIGIT$^+$CD8$^+$ T-cells in PLWH on ART. Thus, we propose CD155 as a potential novel immunotherapeutic target for PLWH on ART.

PO-13. DEVELOPMENT OF AN INTESTINAL EXPLANT MODEL FOR THE STUDY OF TARGETED STRATEGIES DIRECTED TO TISSUE RESERVOIRS

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Introduction: Viral persistence in PLWH despite ART is characterized by the presence of viral reservoir cells, where the gastrointestinal (GI) tract represents a recognized anatomical reservoir. The paucity of samples from PLWH, however, limits its study. Here, using intestinal explants from uninfected donors, we have established a tissue model to evaluate the impact of HIV infection on immune cell populations, the identification of HIV-reservoir cells, and the action of different Latency Reversal Agents (LRAs) in different key CD4$^+$ T subsets.
Methods: Human intestinal tissue resections were obtained from routine surgeries. To develop the best model, we assayed different times for HIV infection, ART initiation, and LRA treatment, in addition to different doses of IL-2 and IL-7. An extensive flow cytometry panel was used to study changes in main immune populations. Identification of HIV-reservoir cells after ART treatment, when most of the reservoir cells are established, was evaluated by detection of viral reactivation after PMA + Ionomycin treatment. Furthermore, the effect of different LRAs, including Ingenol (ING), Romidepsin (RMD), Panobinostat, AZD5582, IL-15, and the combination of RMD+ING, was evaluated by quantification of intracellular p24 in several populations of CD4$^+$ T cells, including *Naïve* (T_{NA}), Central Memory (T_{CM}), Effector Memory (T_{EM}), Resident Memory (T_{RM}, CD69$^+$ and/or CD103$^+$), Follicular Helper (T_{FH}) and Memory CD127$^+$ ($T_{M\text{-}CD127^+}$).
Results: The optimal model consisted of HIV_{BAL} infection of unstimulated tissue blocks on top of gelatin sponges for 6-9 days, followed by ART treatment for 2 days, and the final addition of LRAs for 1 day. As expected, the longitudinal culture induced the natural depletion of some populations, markedly B and myeloid and plasmacytoid DC cells. HIV caused a significant decline in CD4$^+$ T cells, and a considerable increase in NK cells, changes that were partially reversed following ART addition. HIV-reservoir cells in ART-treated tissue were successfully detected in all CD4$^+$ T populations. However, only the combination of ING+RMD reactivated HIV in T_{CM}, $T_{EM,}$ and $T_{RM\text{-}CD69^+}$ cells; whereas IL-15 was strongly active in $T_{RM\text{-}CD69^+}$ and $T_{M\text{-}CD127^+}$. No significant changes were observed for the remaining LRAs.
Conclusions: Overall, our model recapitulates major attributes of HIV infection, including changes in key immune populations throughout productive and treated infection. Most CD4$^+$ T subsets constituted cell reservoirs after ART, however current LRAs only impacted specific populations. Thus, we present a novel tissue model that might provide significant insights into new strategies specifically designed to target tissue reservoirs.

PO-14. CONTROL DE ÉLITE Y MIARNS: LA INHIBICIÓN DE LOS MIR-99B Y MIR-125A REPRIME LA REPLICACIÓN DE VIH-1

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Introducción y objetivos: Los controladores de élite (EC) representan un modelo natural de cura funcional de la infección por VIH, con cargas virales inferiores a 50 copias/ml durante un tiempo prolongado en ausencia de terapia antirretroviral. Trabajos previos describen perfiles de expresión de miRNA asociados al control de élite en distintas poblaciones celulares. Nuestros objetivos son caracterizar el miRNoma y su papel en la regulación de la expresión en células T CD4 de EC y comprobar funcionalmente el rol de los miARN en el control de la replicación viral.
Métodos: Se secuenciaron el transcriptoma y el miRNoma de 26 muestras de células T CD4 obtenidas de EC (n = 10), pacientes VIH+ antes (NT; n = 8) y después (ART; n = 9) de recibir terapia antirretroviral. Se alineó el miRNoma frente a miRBase v22 y los transcritos al transcriptoma humano (GRCh38) y se realizó un análisis de expresión diferencial (DESeq2). Se representaron las parejas miARN-gen diferencialmente expresados usando Tarbase 8.0/miRTarBase v8 y Cytoscape y se anotaron funcionalmente con KOBAS. Para evaluar la

acción de los miARN *in vitro* se transfectaron inhibidores miRCURY (Qiagen) de los miARN en la línea celular CEM-NKR.CCR5 y se infectaron con el clon NL4-3Ren de VIH-1.
Resultados: Al comparar el grupo ART con los EC, se observa una disminución de la expresión de miR-99b-5p (log_2FoldChange (LFC) = –1,00) y miR-125a (LFC = –0,76) (FDR < 0,05). Comparados con los NT, los EC presentan sobreexpresión de miR-27a-5p (LFC = 1,11) y reducción en 6 miARNs, entre ellos miR-99b-5p (LFC = –1,36) y miR-125a-5p (LFC = –0,97). Analizando los DEGs entre EC y ART, los EC sobreexpresan genes diana de miR-99b-5p (MAFB, CCL3, MMP9, TIMP2 o DUSP1), miR-125a-5p (CDKN1A, LAMP1, SOD2, BBC3, CSRNP1, NBEAL2) o de ambos miARNs (DPM2, FLNA, THSB1, RSP2). La reducción de la infección por los inhibidores de los distintos miRNA es del 17,6% [9,3-25,1%] (media geométrica [intervalo de confianza]) para miR-99b-5p, 16,3% [6,2-25,3%] para miR-125a-5p y 21,4% [15,5-26,9%] con ambos inhibidores combinados.
Conclusiones: Hay una disminución de la expresión de los miR-99b-5p y miR-125a-5p en los EC en comparación con NT o ART. El transcriptoma de los EC muestra sobreexpresión de algunas de sus dianas génicas, anotadas en KEGG como parte de vías de señalización de p53, TNF o fagosoma. La inhibición de estos miARNs en células CEM-NKR.CCR5 disminuye la producción viral de VIH-1.

PO-15. CD8+ T CELL AND DENDRITIC CELL INTERACTION IN LYMPH NODES FROM PEOPLE LIVING WITH HIV: IMPLICATIONS FOR HIV-1 CONTROL

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Introduction and objectives: Plasmacytoid dendritic cells (pDCs) play an important role in HIV spontaneous control through their capacity to produce type I interferon. This was principally described in peripheral blood; however, what is occurring in tissues is barely known. Additionally, CD141+ myeloid dendritic cells (mDCs) are one of the main responsible for CD8+ T cell co-stimulation; however, its role in HIV-specific response is mostly unknown. Hence, the objective of this study was to investigate the cooperation of pDCs, CD141+ mDCs and CD8+ T cells in human lymph nodes (LN) to study the effect of this interaction in the control of HIV viremia.
Methods: Inguinal LN biopsies were obtained from ART *naïve* people living with HIV (PLWH), one part of the tissue was disaggregated and cells were obtained for flow cytometry; the other part was frozen and included in OCT for immunostaining and the following analysis by confocal microscopy and histocytometry. Additionally, *in vitro* experiments were performed with CD8+ T cells, pDCs and CD141+ mDCs isolated from peripheral blood of healthy donors and ART *naïve* PLWH. Here, pDCs and CD141+ mDCs were pre-stimulated with toll-like receptor agonists for 18 hours, then they were co-cultured with CD8+ T cells for 6 hours in the presence of SEB or Gag peptides and T cell response was measured by flow cytometry.
Results: First, flow cytometry analysis revealed an inverse correlation between LN pDC percentages with plasma viral load. Moreover, the percentages of pDC and CD141+ mDC subsets were also positively associated with follicular CD8+ T cell frequency. These correlations suggested an interaction in LN. In fact, analyzing the frequencies of B cells, CD4+ and CD8+ T cells, pDCs and CD141+ mDCs by confocal microscopy, histocytometry analysis showed that DCs were mainly located out of the follicles. The observed colocalization of CD8+ T and DC cell subsets indicates an in situ functional interaction between CD8+ T cells, pDCs and CD141+ mDCs in LN of PLWH. Lastly, we observed a higher cytokine production and cytotoxic capacity by CD8+ T cells through the cooperation of pDCs and CD141+ mDCs by co-culture experiments, comparing with CD8+ T cells alone or co-cultured only with pDCs.
Conclusions: There is an interaction between pDCs, CD141+ mDCs and CD8+ T cells in LN from ART *naïve* PLWH. The interaction with activated pDCs and CD141+ mDCs increases antigen-specific CD8+ T cell response. This cooperation axis has implications for immune therapeutic strategies aimed to HIV cure.

PO-16. BIOCOMPATIBLE CARRIERS FOR ERADICATING HIV RESERVOIRS *IN PLWH*

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Introduction: Nowadays, for most of the people living with HIV (PLWH), combination antiretroviral therapy (cART) can effectively suppress HIV replication resulting in undetectable plasma viral load in blood. Nevertheless, HIV reservoirs persist despite cART. In this sense, novel immunotherapeutic approaches are being developed to eradicate HIV. Given the numerous obstacles for sterilizing HIV, biomaterials have recently been considered a platform with potential to improve the therapeutic effect of antiretrovirals. Metal-Organic Frameworks (MOFs) are materials composed by metal ions or clusters coordinated to organic ligands, forming extended network structures. Moreover, liposomes are another type of interesting nanocarriers. They are spherical structures formed by a hydrophobic phospholipid bilayer and an inner aqueous polar region, which let them to host both hydrophilic and hydrophobic compounds. Both systems are promising carriers for eradicating HIV reservoirs. The main goal of this work is the use of these systems as carriers of triple antiretroviral drugs in combination with selected TLR ligands. Selected TLR agonists will permit the activation of innate immune response and clear HIV reservoirs.
Methods: A triple combination of antiretroviral drugs consisting of bictegravir/nevirapine + tenofovir + emtricitabine, together with Toll-Like Receptors (TLRs) agonists: TLR-4 (MPLA), –7 (GS-9620), and –9 (CpG-(ODN 2395) class C), were encapsulated in each of the systems. Drug release experiments were also carried out. Cytotoxicity and apoptosis of both carriers were evaluated in different cell lines (Vero E6, HeLa, U937, Jurkat and THP-1) as well as in Peripheral Blood Mononuclear Cells (PBMCs), isolated from healthy donors. To gain further information about their biocompatibility, *in vitro* hemolytic effect and platelet aggregation assays were performed.
Results: These biomaterials showed a particle size in the nano– and micro-scale (60 nm-50 µm) as well as different physicochemical properties. Data demonstrated a good encapsulation efficiency (> 70%) of the antiretrovirals and TLR agonists, and a slow controlled release for 7 days at different pHs (2.0, 5.5 and 7.4), which could increase the therapeutic effect in tissues of PLWH. Cytotoxicity, apoptosis and necrosis, hemolysis and platelet aggregation results con-

firmed the high biocompatibility of these systems, except at the highest concentrations.
Conclusions: These systems showed high encapsulation efficiency and biocompatibility. Therefore, both structures could be considered potential candidates for eradicating HIV reservoirs in PLWH. Further studies to evaluate the encapsulated drugs and TLR agonists to reach the lymph nodes as well as to modulate the innate immune system in a mice model are on the way.

PO-17. CHARACTERIZATION AND FUNCTIONALITY OF TISSUE-RESIDENT NK CELLS IN MAIN SITES OF HIV PERSISTENCE

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Introduction: NK cells are positioned as important immune players in controlling HIV infection. However, their role in the main tissues where HIV persists, such as the lymphoid tissue and the gastrointestinal tract, is largely unknown. Here, we have characterized NK cells present in relevant tissues, particularly their memory-like and residency properties, and their functionality in killing HIV-infected cells.
Methods: Tissue resections were obtained from routine surgeries. NK cells from two tissues, tonsil (n = 27) and gut (n = 15), were characterized by flow cytometry. We measured the expression of the memory marker NKG2C, the residency markers CD49a, CD69, and CD103, and the Killer-cell immunoglobulin-like receptors (KIRs) KIR2DL1, S1, L2, L3, and S2. To assess the potential of their natural cytotoxicity, we measured the production of CD107a and IFN-γ after co-culturing the tissue cells with the HLA-negative K562 cells (n = 11 for tonsil, and n = 7 for gut). Moreover, using the tonsil explant model (n = 16), the NK phenotype was characterized by flow cytometry after 5-7 days of HIV_{BAL} ex vivo infection.
Results: Tissue-intrinsic distribution of NK cells showed that gut had a higher frequency of $CD56^+$ NK cells (4.7%) compared with tonsils (0.7%). The distribution of the two main NK subsets was similar, showing a predominant population of $CD56^{bright}$ $CD16^-$. However, their minority counterpart ($CD56^{dim}$ $CD16^+$) was the subset more frequently expressing the residency markers CD49a and CD103, KIRs, and the NKG2C marker. Expression of CD69 was associated with $CD56^{bright}$ $CD16^-$ cells across both tissues. Gut tissue had higher expression of the residency markers CD69 and CD103, however, they showed a reduced stimulatory potential compared with tonsils. We detected two main populations that were associated with significant lower levels of HIV infection in the tonsil tissue model; the $CD56^{bright}$ $CD16^-$ $CD103^+$ subset ($r = -0.4711$, $p = 0.036$), and the $CD56^{dim}$ $CD16^+$ $CD69^+$ KIR^+ cells ($r = -0.573$, $p < 0.01$), being the latest significantly expanded in the infected culture ($p = 0.038$). In addition, both subpopulations showed high basal production of CD107a and IFN-γ and heightened functionality after K562 stimulation.
Conclusions: Relevant anatomic sites for HIV present different NK subset distribution and functional capacity. Our research indicates that increased numbers of cytotoxic NK-resident cells might have an important role in HIV control in lymphoid tissue. Hence, strategies aimed at expanding tissue-resident NKs may lead to the development of targeted therapies directed to the main sites of HIV persistence.

PO-18. THE ROLE OF MYELOID-DERIVED SUPPRESSOR CELLS IN ENHANCING HIV INFECTION AFTER A PRIMARY GENITAL TRACT INFECTION

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Objectives: Sexually transmitted infections (STIs) may affect the development and pathogenesis of other STIs, such as the enhancement of HIV replication as a consequence of a genital bacterial infection. Understanding the mechanisms by which STIs enhance early events in HIV acquisition and replication would allow designing preventive strategies. Myeloid-derived suppressor cells (MDSCs) are a diverse population of immature myeloid cells that may exert immune-suppressive effects on other immune cells. Cytokines produced during STIs are similar to those that expand the MDSC population. We therefore hypothesize that MDSCs expand in response to a primary STI, thereby increasing the risk of acquiring a secondary STI such as HIV by suppression of the mucosal immune response.
Methods: Cervical tissue (n = 11) was acquired from patients undergoing cervical surgery. These samples were exposed to *Chlamydia trachomatis* (CT) or GM-CSF plus IL-6 cytokines to assess MDSC expansion and HIV infection by flow cytometry. Furthermore, we obtained paired cervical and blood samples from healthy women (n = 18), or women with acute CT infection (n = 13), Human Papillomavirus infection (HPV) (n = 20), Bacterial Vaginosis (BV) (n = 14) as well as from co-infected patients (n = 12). In these samples, we assessed the cellular immune composition by flow cytometry and the level of eight cytokines, including GM-CSF and IL-6.
Results: *In vitro* exposure of cervical tissue cells to CT or IL-6 plus GM-CSF enhanced subsequent HIV infection (n = 7-9). Moreover, exposure to CT showed a trend towards an increase of the proportion of $CD15^+$ MDSC cells ($p = 0.07$, n = 8) and increased expression of suppressive mediators (i.e. PD-L1). Furthermore, preliminary data from patient cohorts showed changes in the cervical immune environment, including potentially suppressive myeloid subsets in HPV and BV infected patients but limited for CT infected patients. Last, individual cytokine signatures were associated to the cervical and plasma samples for each group of patients.
Conclusions: Enhancement of HIV infection after CT infection and concomitant increase in MDSCs with a suppressive phenotype indicate a potential role for MDSCs in increasing the risk of secondary infection. While HPV and BV groups displayed cellular and cytokine changes that could promote suppressive immune subsets, samples from CT patients showed limited difference in the parameters analyzed so far. Future efforts will include high-dimensional analyses of flow cytometry data and functional analyses to determine the suppressive capacity of cervical MDSCs on other immune cell populations.

PO-19. IMPACT OF HIV RESERVOIR IN THE LOSS OF NATURAL ELITE CONTROL OF HIV-1 INFECTION

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Objectives: HIV-1 elite controllers (EC) are a rare group of people living with HIV (< 1%) who can naturally maintain undetectable levels of viremia in the absence of antiretroviral therapy (ART). Nevertheless, approximately 25% of EC eventually loss virological control.

This has enabled to classify EC in two groups: i) "transient elite controllers" (TC), those who eventually lose viremia control and ii) "persistent controllers" (PC), those who maintain viremia control indefinitely overtime. It is important to identify the factors that lead to HIV disease progression to open new avenues in HIV cure strategies. Several studies have shown that PC and TC present different immunological, proteomic, metabolomic and miRNA profiles but in terms of virological factors, it is essential to deeply characterize the quality of HIV reservoirs to distinguish both phenotypes.
Methods: Genomic DNA from 18 PC (viremia control for more than 23 years), 10 TC (sustained viral load above the detection limit, > 40 HIV RNA copies/mL, during more than one year of follow-up) before losing the control (0.3-2 years) and 41 antiretroviral-treated individuals for a median of 9 years (2-19 years), was isolated from peripheral blood mononuclear cells (PBMCs). Subsequently, the characterization of HIV-1 reservoir was performed using next-generation sequencing techniques, such as full-length individual proviral sequencing (FLIP-seq) and matched integration site and proviral sequencing (MIP-seq).
Results: PC and TC presented significantly lower total, intact and defective proviruses compared to ART-treated individuals. Although no significant difference was found in total proviruses between PC and TC, a trend in TC to have higher defective provirus was observed ($p = 0.072$). Interestingly, the proportion of intact proviruses were significantly higher in TC compared to PC ($p = 0.005$). Moreover, non-clonally expanded intact proviruses were found in TC, showing a higher viral diversity in comparison to PC. Regarding the integration sites, intact proviruses from TC and ART were located in permissive genic euchromatic positions in contrast to PC whose intact proviruses were located in centromeric satellite DNA or zinc-finger genes (ZNF), both associated with heterochromatin features.
Conclusions: PC, TC and ART-treated individuals presented a distinct proviral reservoir landscape in PBMCs. The intact proviruses from TC and ART-treated individuals were located in genic regions in contrast to persistent controllers' intact proviruses that were preferentially integrated in non-genic or pseudogenic regions.

PO-20. AIDS-VIRUS SUPPRESSION FOLLOWING AAV-MEDIATED DELIVERY OF CLOSER-TO-GERMLINE MONOCLONAL ANTIBODIES IN RHESUS MACAQUES

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Introduction: Delivery of potent and broadly neutralizing antibodies (bNAbs) by means of recombinant adeno-associated virus (AAV) is a promising approach for the treatment of HIV infection. We have previously reported three monkeys which, after receiving AAVs encoding a cocktail of neutralizing anti-HIV antibodies during the chronic phase of infection, have shown suppressed viral loads for years and appear to have been functionally cured. Unfortunately, our attempts to create more such functional cures have been severely hampered by the generation of anti-drug antibody responses (ADAs) to the AAV-delivered antibodies. Due to years of affinity maturation, most bNAbs exhibit unusually high levels of somatic hypermutation and accumulate uncommon features that can be seen as 'non-self' by the recipient's immune system. Consequently, unwanted ADAs responses can be raised against the AAV-delivered bNAbs, compromising their efficacy by reducing their concentration and functionality. In this project we have strived to overcome this critical issue by delivering less mutated antibodies, i.e. antibodies closer to their germline.
Methods: In a proof-of-concept experiment, 4 Indian-origin rhesus macaques were experimentally infected with SHIV-AD8. At week 14 post-SHIV infection these monkeys received recombinant AAVs expressing three broadly neutralizing antibodies (DH270, PCIN63 and DH511) that were naturally closer to germline than those we had used previously. *In vivo* circulating antibody and ADA levels were measured over time by ELISA.
Results: Sustained viral load suppression was achieved in two of the four treated monkeys, which is our highest success rate to date (50%). Overlays of viral loads and antibody levels clearly showed the AAV-delivered antibodies as the drivers of the viral load drops. High levels (22-327 µg/mL) of two AAV-delivered antibodies were obtained in three of the four macaques through the 18 weeks of measurements. Two of these three were the successfully suppressed monkeys and the third one showed only transient effects on viral load levels; an escape mutant virus is suspected in this third monkey. This non-suppressed third monkey had the highest viral loads at the time of AAV administration (130,000 RNA copies/mL). The fourth monkey had low antibody levels due to ADAs. Overall ADA levels correlated well with the AAV-delivered antibody levels: the lower the ADAs, the higher the antibody levels.
Conclusions: Our data indicate that the use of closer-to-germline bNAbs may be a viable strategy for avoiding ADAs following gene therapy with AAV-bNAb vectors and support their potential for improved long-term suppression of viral loads with the AAV-antibody approach.

Sesión Póster Oral 3 – Pósteres Orales *Continuum* de atención clínica – 29 de noviembre – 15:00-16:45h

PO-21. CRIBADO DIRIGIDO DE LA INFECCIÓN VIH EN LOS SERVICIOS DE URGENCIAS. PROYECTO VHIGILA

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Introducción: En nuestro país se diagnostican unos 10 casos de infección por VIH diarios. A pesar de ser una enfermedad prevenible, el goteo de nuevas infecciones es incesante, en una infección que cursa muchos años de manera oculta. Es fundamental establecer diversas estrategias dirigidas a identificar la población infectada.
Objetivos: Hasta un 30% de los pacientes diagnosticados por VIH, podrían haber sido identificados más precozmente si en un Servicio de Urgencias (SU) se hubiera realizado un test diagnóstico en un contexto médico consensuado. El reciente consenso SEMES-GESIDA 2020 recomienda realizar serologías de VIH en los SU en 6 escenarios clínicos muy concretos: presencia de ETS, profilaxis post exposición (PPE), práctica de chem-sex (CS), síndrome mononucleósido (SMN), neumonía comunitaria (NC) en menores de 65 a, herpes zoster (HZ) en menores de 65 a. El presente estudio analiza los resultados de la implementación del mencionado consenso, mediante un protocolo dirigido (Proyecto VIHGILA-SOCMUE).

Métodos: Se incluyen 10 SU de hospitales de Cataluña. En todos los hospitales se realiza una formación específica del personal médico, enfermería y servicio de microbiología: explicando los detalles y manera concreta de aplicar el consenso. En cada uno de los SU hay un médico y enfermera responsable para implementar el protocolo, realizando un control estricto de todos los procedimientos. Los datos se actualizan semanalmente con un seguimiento centralizado. Se exponen los resultados globales y también por cada uno de los 6 escenarios especificados.
Resultados: Tras 60 semanas de seguimiento (1 junio 2021-30 agosto 2022), se han realizado 5.959 serologías VIH y se han diagnosticado 54 nuevos pacientes con VIH (0,9%). 33/54 (61%) de los nuevos diagnósticos se producen en los 6 escenarios descritos: 5 casos de VIH sobre 1211 PPE (0,4%), 7/796 ETS (0,8%), 13/694 NC (1,8%), SMN 5/257 (1,9%), CS 2/35 (0,7%), HZ 1/149 (0,6%), pacientes con otras patologías 21/2817 (0,7%).
Conclusiones: La aplicación del consenso SEMES muestra una elevada eficacia diagnóstica: casi un 1% de las serologías son positivas para VIH. Estos porcentajes están 10 veces por encima de los porcentajes considerados como eficientes (> 0,1%) para la realización de un cribaje. La realización de serología pacientes con NC y SMN muestra un altísimo nivel de eficacia, cercano al 2%. A la luz de estos resultados, los SU se muestran como un lugar óptimo para cribar y diagnosticar infección por VIH. Es preciso formar a los equipos sanitarios para implementar protocolos de detección de VIH en los SU.

PO-22. LA OPORTUNIDAD PERDIDA DE DIAGNÓSTICO PRECOZ DEL VIH EN LAS ESTRATEGIAS DE CRIBADO DIRIGIDAS ESTRICTAMENTE A LA ELIMINACIÓN DEL VHC

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Introducción: La llamada de la OMS a redoblar los esfuerzos de eliminación de las hepatitis víricas y el plan nacional de eliminación de la hepatitis C ha llevado a diversos grupos a la estrategia de realización de cribados poblacionales y dirigidos, encaminados unilateralmente a la eliminación del VHC.
Objetivos: Constatar el número de casos de VIH que hubieran quedado sin diagnóstico, si el cribado poblacional se hubiera destinado solo a la detección del VHC.
Métodos: El programa departamental de cribado Crivalvir-Focus del departamento de salud Hospital General de Valencias está enfocado al diagnóstico precoz de los virus transmitidos por sangre (VIH; VHB; VHC) en la población que acude a los servicios sanitarios. Diagnosticar nuevos casos y "rescatar" aquellos diagnosticados previamente pero que están sin controles y tratamiento El proyecto se realizó en dos fases: previa a la prepandemia SARS-CoV-2 (febrero 2019 febrero 2020) y durante las olas pandémicas (septiembre 2020-enero 2022).
Resultados: Se han cribado 31.995 personas, 52% mujeres y 15% foráneos, detectándose 112 personas con infección activa por el VHC, prevalencia del 0,35%. De ellos el 70% eran nuevos diagnósticos, en el otro 30% se constató seropositividad anterior, pero sin seguimiento. La prevalencia fue mayor en hombres que en mujeres (0,51 *vs.* 0,20%) y en foráneos frente a nacidos en España (0,60 *vs.* 0,32%) La mayor prevalencia la encontramos en las franjas etarias de los 45 a 64 años, con un 0,75%. De no haber cribado también la serología VIH en el programa hubiéramos dejado sin diagnosticar 56 casos (84% desconocidos) de ellos 69% hombres y 41% foráneos. Prevalencia global del 0,17%, mayor en las franjas etarias de 25-54 años. Prevalencia superior en hombres que en mujeres (0,25 *vs.* 0,11%) y en foráneos con respectos a autóctonos (0,58 *vs.* 0,11%).
Conclusiones: Nuestros datos reflejan que si hubiéramos optado por un cribado dirigido solamente al diagnóstico del VHC por cada hepatitis C diagnosticada se hubiera dejado sin diagnosticar 0,50 casos de VIH. La pérdida de oportunidades para el diagnóstico de otros virus transmitidos por sangre en los cribados poblacionales únicamente para el VHC es manifiesta.

PO-23. CARACTERÍSTICAS DE UNA COHORTE DE PACIENTES DIAGNOSTICADOS DE PRIMOINFECCIÓN POR VIH EN UNA UNIDAD DE ITS EN LA ERA PREP

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Introducción: El diagnóstico de la primoinfección VIH supone un reto, siendo las clínicas de ITS un lugar idóneo para realizarlo. En 2020 se implementó la PrEP, pero el acceso inicial fue limitado por la pandemia SARS-CoV-2. El objetivo de este estudio es describir las características clínico-epidemiológicas de los pacientes diagnosticados con primoinfección VIH en la Unidad ITS Drassanes-Vall d'Hebron en este nuevo contexto.
Métodos: Se revisaron las historias clínicas de los diagnósticos de VIH en la unidad desde enero 2020 hasta junio 2022, y se seleccionaron las primoinfecciones, definidas como estadio Fiebig ≤ V. Se recogieron variables demográficas, clínicas, de laboratorio, tiempo hasta el inicio de TAR y relación con el programa PrEP. Se calcularon medianas para las variables cuantitativas y se utilizó el test de Mann Whitney para realizar comparaciones.
Resultados: Hubo 22 primoinfecciones de un total de 80 nuevos diagnósticos (28%), ninguna durante los meses de marzo a junio 2020 (5 nuevos diagnósticos de VIH en ese periodo). El 95% eran HSH, con edad mediana de 33 años (RIC 25-37), mayoritariamente españoles o latinoamericanos. El 77% reportaba síntomas, principalmente fiebre, exantema y odinofagia. En 9 pacientes se realizó un test rápido en sangre (Determine™ HIV Early Detect), que fue positivo en 5 casos (sensibilidad 56%). La serología fue positiva en todos los pacientes menos uno, cuyo diagnóstico se obtuvo por carga viral. El tiempo mediano hasta inicio de TAR fue 3 días (RIC 1-4), menor cuando se obtuvo el positivo por test rápido frente a la serología (2 *vs.* 5 días, p = 0.01). La carga viral mediana fue 880.000 copias/ml (rango 3.770-65.200.000) y los CD4 medianos 420/ml (RIC 330-585). Respecto a la PrEP, 6 pacientes la habían solicitado con más de 3 meses de antelación y 10 pacientes se diagnosticaron durante una visita del programa: 5 en la valoración basal, 4 en la visita de inicio y uno 6 semanas después de haber iniciado (se detectaron las mutaciones de resistencia M184V y K65R), sin ninguna otra infección en seguimientos posteriores.
Conclusiones: Uno de cada 3 nuevos diagnósticos fue una primoinfección y casi la mitad de ellas se dieron en una visita del programa PrEP. No se detectaron primoinfecciones durante el confinamiento por COVID-19. El TAR se inició muy precozmente, especialmente cuando se obtuvo un diagnóstico al momento mediante pruebas rápidas, aunque su sensibilidad fue baja. El retraso de inicio PrEP por lista de espera pudo condicionar nuevas infecciones.

PO-24. RESISTENCIAS TRANSMITIDAS EN PACIENTES *NAÏVE*. ACTUALIZACIÓN 2019-2021

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Introducción: CoRIS Resistencias es un programa establecido desde 2007 para la evaluación de la resistencia transmitida a los antirretrovirales (TDR). En este trabajo se presenta la actualización de los datos de TDR en pacientes de nuevo diagnóstico para el periodo 2019-2021.
Métodos: Se incluyeron los nuevos diagnósticos con secuencias fasta disponibles en los centros CoRIS. Tras el control de calidad de los fasta, se investigaron las mutaciones en RT y Pro asociadas a TDR (herramienta CPR-Stanford, basada en Bennett, 2009). Para la integrasa, también utilizamos la herramienta CPR-Stanford. Además, evaluamos las resistencias clínicamente relevantes (nivel intermedio o resistente) a los fármacos actualmente recomendados como tratamiento de primera línea en las guías de GESIDA, así como a los NNRTIs EFV, DOR y RPV.
Resultados: Se analizaron un total de 1.857 pacientes, 758 (2019), 567 (2020) y 532 (2021); de ellos, se dispuso de datos de integrasa en 552 pacientes, 264 (2019), 167 (2020) y 121 (2021). La TDR en el periodo 2019-2021 fue: 3,7% para los NRTI, 6,02% para los NNRTI, 0,97% para los IP y 0,37% para los INI. En 2021 fue del 3,2% para los NRTI, del 5,9% para los NNRTI, del 0,75% para los IP y del 0% para los INI. La resistencia clínicamente relevante a los fármacos de primera línea en el periodo 2019-2021 fue del 1,3% para TDF (de los cuales el 1,2% eran Intermedios), el 2% para ABC, el 0,8% para 3TC/FTC, el 6,4% para EFV, el 2,6% para DOR (1,5% I), el 7,1% para RPV, el 2% para RAL (todos Intermedios), el 0,18% para BIC y DTG (n = 1,S153F) y en 2021, fue del 1,2% para TDF (todos intermedios), del 1,7% para ABC (todos intermedios), del 0,5%para 3TC/FTC, del 6,2% para EFV, del 2% para DOR (1,3% intermedio), del 8,8% para RPV (6,7% intermedio), del 2,4% para RAL (todos intermedios); BIC, DTG y DRV no presentaron ningún nivel de resistencia.
Conclusiones: Como en años anteriores, la mayor prevalencia de resistencias transmitidas se produjo para los INNR, siendo doravirina el fármaco de esta familia con menores niveles de TDR. La resistencia transmitida a los IPs, INIs y 3TC/FTC continúa en niveles muy bajos, sin que ningún paciente presente resistencia completa a los inhibidores de la integrasa de 2ª generación o darunavir.

PO-25. HIV CARE INTERRUPTION AMONG HIV-POSITIVE INDIVIDUALS IN SPAIN, 2004-2020

R. Izquierdo[1], M. Rava[1], E. Orviz[2], J.A. Pineda[3], Á. Mena[4], L. Romero[5], R. Muga[6], R. Rubio[7], J.A. Iribarren[8], I. Jarrín[1] and Cohort of the Spanish HIV/AIDS Research (CoRIS)[9]

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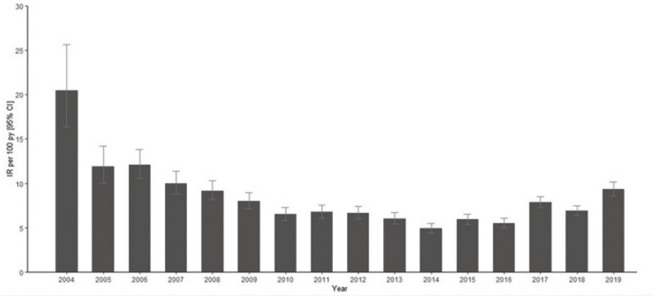
Objectives: We aimed to estimate the incidence rate of HIV care interruption and its evolution over a 16 year-period, as well as to identify the associated risk factors among HIV-positive individuals from the cohort of the Spanish AIDS Research Network (CoRIS) during 2004-2020.
Methods: We included antiretroviral-*naïve* individuals aged ≥ 18 years at enrolment, recruited between January 1, 2004, and August 30, 2019, and followed-up until November 30, 2020. Interruption of care was deemed to have occurred when more than 15 months had elapsed between two consecutive visits to the clinical centre. When more than one interruption of care was observed for an individual, only the first one was considered. We calculated the incidence rate (IR) of interruption of care, overall, annually and according to sociodemographic and clinical characteristics at enrolment, and used multivariable Poisson regression models to estimate adjusted incidence rate ratios (IRR) and their 95% confidence intervals (CI) for the association between potential risk factors and the rate of care interruption.
Results: Of 15,274 individuals included, 84% were men and median age was 35 years. During 76,384 person-years (py) of follow-up, 5,481 individuals discontinued their HIV care [IR: 7.2/100 person-years (95%CI 7.0-7.4)]. The annual IR gradually decreased from 20.5/100 py (95%CI 16.4-25.6) in 2004 to 4.9/100 py (95%CI 4.4-5.5) in 2014. Thereafter, a slight increase was observed between 2015 and 2018, reaching 9.3/100 py (95%CI 8.6-10.2) in 2019 (Fig.). Independent risk factors for interruption of care included younger age (adjusted IRR 1.91; 95%CI 1.71-2.14 for 18-29, 1.52; 1.36-1.69 for 30-39 and 1.19; 1.06-1.34 for 40-49 *versus* ≥ 50 years), lower educational level (1.10; 1.00-1.22 for no/primary *versus* university studies), having contracted HIV infection through injecting drug use (1.74; 1.53-1.97) or heterosexual intercourse (1.12; 1.04-1.22) compared to men who have sex with men, having been born outside of Spain (1.49; 1.27-1.75 for Eastern Europe, 2.19; 1.96-2.45 for sub-Saharan Africa, 1.50; 1.20-1.89 for Northern Africa, and 1.47; 1.37-1.58 for Latin America), CD4 count > 200 cell/uL (1.10; 1.01-1.20 for 200-350 and 1.21; 1.12-1.31 for > 350 *versus* < 200 cells/ml) and viral load < 100,000 (1.17; 1.09-1.27 for < 10,000 and 1.08; 1.01-1.16 for 10,000-100,000 *versus* > 100,000 copies/ml), and co-infection with HCV (1.24; 1.11-1.38) at enrolment.



Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
IR per 100 py	20.5	11.9	12.1	10.0	9.2	8.0	6.5	6.8	6.7	6.0	4.9	5.9	5.5	7.9	6.9	9.3
95% CI	16.4	10.0	10.5	8.8	8.2	7.1	5.8	6.1	6.0	5.4	4.4	5.4	5.0	7.3	6.4	8.6
	25.6	14.2	13.8	11.4	10.3	8.9	7.3	7.5	7.4	6.7	5.5	6.5	6.1	8.5	7.5	10.2

Figure 1. Annual incidence rates (IR; 95% CI) interruption of care per 100 persons-year of follow-up, CoRIS cohort, 2004-2020.

Conclusions: We recommend to put a spotlight on patients at high risk for interruption of care, and devise effective strategies to reengage those who interrupted care as a result of the COVID-19 pandemic.

PO-26. EFFECTIVENESS OF DOLUTEGRAVIR + LAMIVUDINE IN REAL-WORLD STUDIES IN PEOPLE WITH HIV-1 WITH M184V/I MUTATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Kabra[1], C. Allavena[2], A.G. Marcelin[3], S. di Giambenedetto[4], J. Pasquau[5], N. Gianotti[6], M. Turner[7], C. Harrison[7], T. Wynne[7], G. Verdier[8], C. Parry[1], B. Jones[1], C. Okoli[1], J. Priest[9] and E. Letang[10]

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Introduction and objectives: Antiretroviral regimens are typically not recommended if resistance to components is known or suspected, but historical resistance results are not always available. In phase 3 trials evaluating switch to dolutegravir/lamivudine (DTG/3TC), absence of historical resistance results (n = 294; pooled TANGO/SALSA) or presence of archived M184V/I mutations (TANGO, n = 4; SALSA, n = 5) did not impact virologic efficacy. This meta-analysis describes virologic failure (VF) at Weeks 24, 48, and 96 using real-world data from people with HIV-1 (PWH) receiving DTG+3TC in a suppressed switch setting, with historical RNA– or archived proviral DNA-detected M184V/I mutation.

Methods: A systematic literature review was performed following PRISMA guidelines. Embase®, Ovid MEDLINE®, MEDLINE® In-Process, and Cochrane library (January 2013-March 2022) and conference archives (2016-2021) were searched for real-world studies reporting virologic outcomes for PWH receiving DTG+3TC. A targeted literature review was performed to identify randomized controlled trials (RCTs) assessing M184V/I impact on DTG+3TC efficacy. Studies were screened for populations reporting historical M184V/I mutations before DTG+3TC initiation. Fixed– and random-effects model analyses were conducted from real-world studies (primary objective). Sensitivity analyses were performed using RCT data (secondary objective).

Results: Of 3,492 publications and 198 conference abstracts identified, 5 real-world studies met all criteria and were analyzed (Table); 5 relevant RCTs were also identified. Proportions of PWH with historical M184V/I estimated to have VF at Weeks 24, 48, and 96 were low in real-world and RCT analyses based on VF events (real-world: 3/186 [1.61%], 7/237 [2.95%], 7/186 [3.76%], respectively; RCT: 0/38 [0%], 2/93 [2.15%], 0/34 [0%], respectively; Fig.), with no reported treatment-emergent resistance.

Conclusions: Although M184V/I incidence was low, real-world studies of PWH with historical M184V/I receiving DTG+3TC identified low VF incidence through 96 weeks, as did sensitivity analyses from RCTs. Though not indicated in PWH with known resistance mutations, this meta-analysis provides data on outcomes with DTG+3TC in PWH with incomplete history or if archived M184V/I is inadvertently missed.

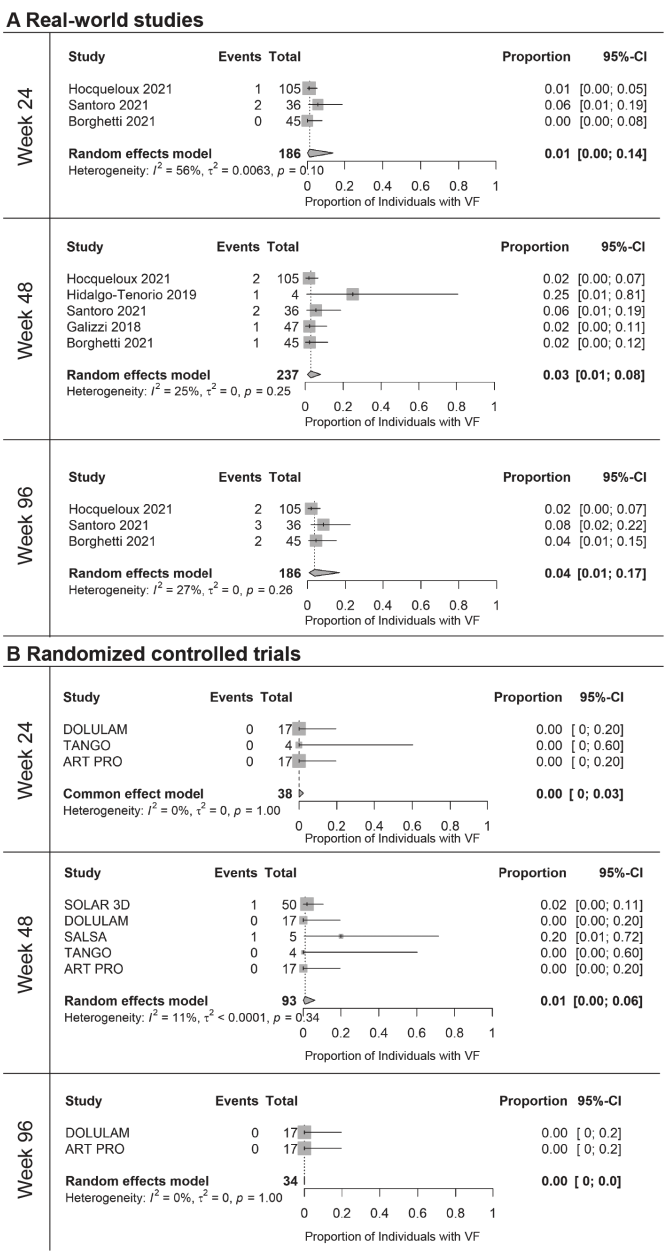

Figure. Meta-analysis estimates of proportions of VF at Weeks 24, 48, and 96 in people with HIV-1 and reported M184V/I receiving DTG+3TC from **(A)** systematic literature review–identified real-world studies and **(B)** targeted literature review–identified randomized controlled trials, inclusive of all VF definitions.

Proportions were log-transformed, or arcsine-transformed if any studies reported zero events. DTG+3TC, dolutegravir + lamivudine; VF, virologic failure.

PO-27. PREGNANCY OUTCOMES AND ANTIRETROVIRAL TREATMENTS AMONG WOMEN WHO ARE DIAGNOSED WITH HIV DURING PREGNANCY IN THE CORIS COHORT

I. Suárez-García[1], B. Alejos[2], C. Moreno[3], R. Izquierdo[3], J.R. Blanco[4], E. Bernal[5], D. Corona-Mata[6], P. Galindo[7], A. Antela[8], V. Hernando[3] and I. Jarrín[3]

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Introduction and objectives: To describe the clinical characteristics, pregnancy outcomes and trends in prescription of antiretroviral treatments (ARTs) among women who were diagnosed with HIV during pregnancy in the Cohort of the Spanish HIV/AIDS Research Network (CoRIS).

Methods: We analysed women aged 18-50 years who were diagnosed with HIV during pregnancy and were enrolled in the cohort during the years 2004-2019. We described first-line ARTs prescribed to those whose pregnancies resulted in a delivery by time period.

Results: During the study period, 1,840 women aged 18-50 years were enrolled in CoRIS. Of these, 154 (8.4%) were diagnosed with HIV during pregnancy and were included in the study. Their clinical characteristics and pregnancy outcomes are shown in the table. Among 145 pregnancies that resulted in a delivery, 121 (83.4%) had viral load < 50 copies/ml at week 36 of pregnancy. The proportion of caesarean sections

was 46.5% among all deliveries, and 46.3% among those with viral load < 50 copies/ml at week 36 of pregnancy. Sixty (41.4%) women had induced labour. Median gestational age at delivery was 39.4 [IQR: 38.1; 40.4]. There were no neonatal deaths, 2 infants were diagnosed with HIV and median birth weight was 3030 [IQR: 2,510; 3,380] grams. ART was prescribed to 141 women whose pregnancies resulted in a delivery; their first-line treatments are shown in the figure.

Characteristics and pregnancy outcomes of 154 women who were diagnosed with HIV during pregnancy

	N (%)
Age at pregnancy, years (Median [IQR])	29.4 [25.2-33.1]
Country of origin	
Spain	43 (27.9%)
Other	110 (71.5%)
Unknown	1 (0.6%)
Educational level	
None/primary	76 (49.3%)
Secondary/university	38 (24.7%)
Other	8 (5.2%)
Unknown	32 (20.8%)
HIV transmission mode	
Heterosexual intercourse	144 (93.5%)
Other	6 (3.9%)
Unknown	4 (2.6%)
Late presenter	
No	67 (43.5%)
Yes	69 (44.8%)
Unknown	18 (11.7%)
Time of HIV diagnosis during pregnancy	
First trimester	97 (63.0%)
Second trimester	40 (26%)
Third trimester	15 (9.7%)
At delivery	2 (1.3%)
Pregnancy outcome	
Delivery	145 (94.2%)
Voluntary termination	6 (3.9%)
Miscarriage	1 (0.6%)
Unknown	2 (1.3%)

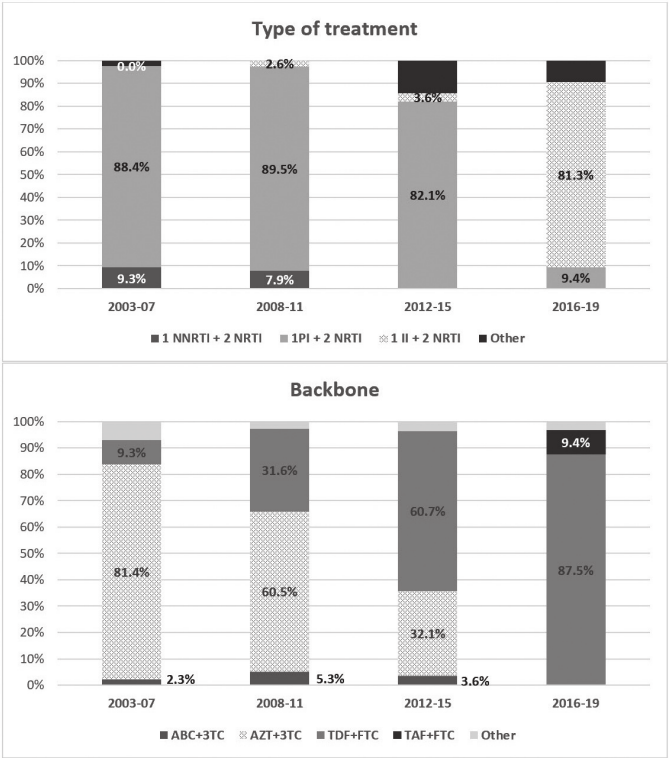

Figure. Trends in prescription of first-line antiretroviral treatments in 141 women who were diagnosed with HIV during pregnancy and had a delivery

Conclusions: Women who were diagnosed with HIV during pregnancy were predominantly foreign-born and with low educational level. More than a third were diagnosed after the first trimester, and 83.4% had undetectable viral load at week 36 of pregnancy. There was a very high proportion of cesarean sections, even among women with undetectable viral load. During the later years, integrase inhibitors and TDF/FTC have been the most prescribed initial ARTs.

PO-28. INCREASING THE DIAGNOSIS OF CA-MRSA INFECTION IN PLWH WHO ENGAGE IN CHEMSEX IN BARCELONA

L. de la Mora Cañizo, M. Martínez-Rebollar, C. Pitart, L. Morata, A. Ugarte, E. de Lazzari, A. Vergara, J. Bosch, I. Roca, M. Piquet, A. Rodríguez, M. Laguno, J. Ambrosioni, B. Torres, A. González-Cordón, A. Inciarte, A. Foncillas, J. Riera, I. Fuertes, I. Chivite, E. Martínez, J.L. Blanco, A. Soriano and J. Mallolas

Hospital Clínic de Barcelona, Barcelona.

Introduction: There are no data on community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections in the context of the chemsex phenomenon. This study aimed to characterize CA-MRSA-related infections in a cohort of PLWH who engage in chemsex.
Methods: We analyzed CA-MRSA infections diagnosed in a cohort of PLWH who engage in chemsex between February 2018 and January 2022 at the Hospital Clinic of Barcelona. Epidemiological, behavioral and clinical variables were assessed. Mass spectrometry identification and antimicrobial susceptibility testing were performed on MRSA isolates. Pulse field electrophoresis was used to assess the clonality of the MRSA strains. The presence of Panton-Valentine leukocidin was also investigated.
Results: Among the cohort of 299 participants who engage in chemsex, 25 (8%) with CA-MRSA infections were identified, 9 at baseline and 16 with incident cases; the cumulative incidence was 5.5% (95%CI: 3.2-8.8%). The most common drugs were methamphetamine (96%) and GHB/GBL (92%). Poly-consumption and slamming were reported by 32% and 46%, respectively. CA-MRSA was isolated from the infection sites of 20 participants, and CA-MRSA colonization was confirmed in the remaining five persons. 71% had used antibiotics in the previous year. All participants presented with skin and soft tissue infections, 28% required hospitalization, and 48% had recurrence. Of the 23 MRSA isolates further studied, 19 (82,6%) belonged to the same clone. Panton-Valentine leukocidin was detected in all isolates.

CA-MRSA infections in a cohort of PLWH who engage in chemsex

Health care-associated risk factors	n (%)
Antibiotic use (previous yr) (N = 25)	19 (76%)
Surgery (previous yr) (N = 25)	1 (4%)
Hospitalization or long-term care facility admission, at least a 1 night stay (N = 25)	3 (12%)
Clinical Characteristics	
SSTI (N = 25)	25 (100%)
Bacteriemia (N = 25)	3 (12%)
Pneumonia (N = 25)	1 (4%)
SSTI clinical presentation	
Abscess	17 (68%)
Cellulitis	14 (56%)
Folliculitis	2 (8%)
Furunculosis	7 (28%)
SSTI localization	
Head/neck	4 (16%)
Trunk	5 (20%)
Upper extremities	4 (16%)
Groin/buttocks/perineum	11 (44%)
Lower extremities	11 (44%)

CA-MRSA infections in a cohort of PLWH who engage in chemsex *(cont.)*	
Other clinical characteristics	
Hospitalization (N = 25)	7 (28%)
Recurrence* (N = 21)	10 (48%)
Colonization (N = 24)	13 (54%)
Nasal (N = 13)	12 (92%)
Perineum (N = 13)	1 (8%)
Treatment	
Incision/ drainage/ surgery (N = 25)	13 (52%)
No treatment (N = 25)	1 (4%)
Antibiotic (N = 25)	24 (96%)

SSTI: Skin and soft tissue infection. *More than one episode during the follow-up period, after the first diagnosis

Conclusions: PLWH engaged in chemsex may present with CA-MRSA infections. Clinical suspicion and microbiological diagnosis are required to provide adequate therapy, and CA-MRSA prevention interventions should be designed.

PO-29. MOXIFLOXACINO COMO PRIMERA LÍNEA DE TRATAMIENTO EN URETRITIS POR *MYCOPLASMA GENITALIUM* EN HOMBRES QUE TIENEN SEXO CON HOMBRES

P. Álvarez López, J. García Pérez, M. Arando Lasagabaster, V. Descalzo Jorro, A. Monforte Pallarés, Y. Hoyos Mallecot, J. Trejo Zahinos, E. Sulleiro Igual, F. Zarzuela Serrat, E. Ruiz Martí, D. Martínez Rascón, L. López Pérez, J. Pilarte Villanueva, D. Téllez Velasco y V. Falcó Ferrer

Hospital Universitari Vall d´Hebron, Barcelona.

Introducción y objetivos: La resistencia del *Mycoplasma genitalium* (MG) a la azitromicina (AZT) ido aumentando en los últimos años. Sin embargo, las guías internacionales continúan recomendando la AZT como tratamiento de primera línea de uretritis no complicadas por MG, manteniendo el moxifloxacino como segunda línea. El objetivo de este estudio fue analizar las características de los pacientes con uretritis por MG y los porcentajes de curación con AZT y moxifloxacino.
Métodos: Se analizaron todos los pacientes que consultaron por uretritis en la unidad de ITS Drassanes-Vall d'Hebron durante el año 2021.
Resultados: Quinientas cuarenta personas resultaron positivas para MG en PCR de orina, exudado uretral, vagina, recto o faringe. Tenían uretritis por MG 67 (62,7% con secreción uretral, 37,3% sin ella). Todas fueron hombres cisgénero, de los cuales 25,4% tenían sexo exclusivamente con mujeres y 74,6% hombres que tenían sexo con hombres (HSH) exclusivamente o también con mujeres. El 14,9% tenían infección por VIH. Previo al diagnóstico de uretritis por MG 14 pacientes (20,9%) ya habían recibido antibiótico, mayoritariamente doxiciclina (28,6%). Dos presentaban coinfección con gonococo y cinco con *Chlamydia*. Tras el diagnóstico la mayoría recibieron doxiciclina + AZT (67,2%), obteniendo un porcentaje de curación del 28,9% (test de cura [TOC] no realizado en el 20%), seguido de doxiciclina + moxifloxacino (11,9%), con un porcentaje de curación del 75% (TOC no realizado en el 25%). Veintiocho precisaron segunda línea de tratamiento por uretritis recurrente, más frecuentemente con moxifloxacino (57,1%), con un porcentaje de curación del 56,3% (TOC no realizado en el 31,3%), seguido de doxiciclina + moxifloxacino (17,9%), con un porcentaje de curación del 60% (TOC no realizado en el 20%). Se objetivaron diferencias en cuanto al porcentaje de pacientes HSH que fracasaron a la AZT (55,6% TOC positivo, 19,4% no realizado) respecto a no HSH (23,1% TOC positivo, 23,1% no realizado), aunque no estadísticamente significativas (p = 0,098). Cuatro pacientes precisaron tercera línea: dos se curaron tras pristinamicina y doxiciclina + pristinamicina respectivamente. El tercero recibió minociclina y presentó síntomas antes del TOC, curándose tras cuarta línea con pristinamicina. El cuarto se consideró reinfección de pareja habitual no tratada y recibió nuevamente moxifloxacino, con nueva recurrencia, y curándose tras pristinamicina.
Conclusiones: El porcentaje de pacientes HSH con uretritis por MG que fracasan a la AZT en nuestro medio es muy superior al de moxifloxacino, por lo que podría plantearse como primera línea de tratamiento. Un alto porcentaje de personas no acuden al TOC, lo que no permite confirmar la curación.

PO-30. MIGRANTES CON INFECCIÓN VIH EN SITUACIÓN IRREGULAR EN LA COMUNIDAD DE MADRID Y LA NECESIDAD DE IMPLEMENTAR NUEVOS MODELOS ASISTENCIALES

P. Ryan[1], N. Deihim Rahampour[2], G. Cuevas Tascón[1], S. Manzano Varela[1], J. Valencia la Rosa[1], B. Fernández Gómez[1], S. Estévez Alonso[1], D.E. Brown Lavalle[1] y A. González Baeza[3]

[1]Hospital Infanta Leonor, Madrid. [2]Fundación Estatal Salud, Infancia y Bienestar Social, Madrid. [3]Facultad de Psicología. Universidad Autónoma de Madrid, Madrid.

Objetivos: Describir el perfil actual de personas con VIH (PVIH) migrantes en situación irregular, analizando su situación social, clínica y cómo les afecta la dificultad para acceder al sistema sanitario.
Métodos: Las PVIH fueron atendidos en la consulta de VIH de un hospital de Madrid. El circuito de derivación se realizó directamente desde una ONG a la consulta de VIH. Todos las PVIH recibieron una valoración por especialista en Enfermedades infecciosas y una valoración por una trabajadora social. Se recogieron variables de interés demográfico, social y clínico para realizar un análisis.
Resultados: Durante el periodo del estudio 486 PVIH migrantes en situación irregular fueron atendidos en la consulta. La mediana de edad 32 (28-37) años, 420 (86%) eran varones cis, 364 (85%) afirmaron orientación homosexual y 427 (88%) eran hispanos. A su llegada, la mayoría no tenía red social de apoyo 199/409 (49%), 192/383 (50%) tenían estudios universitarios y 318/362 (88%) presentaban barreras para acceder al sistema sanitario. El 46% (217/475) habían sido diagnosticados de una infección de transmisión sexual (ITS) en el último año. Un total de 68 PVIH (14%) consumió algún tipo de droga en el último año. La mediana de duración de la infección por el VIH fue de 5 (3-8) años (transmisión del VIH fue por vía sexual 97%). De los que tomaban TARV a su llegada, 78 personas (22%) lo tuvo que discontinuar después de cruzar la frontera por falta de acceso a una consulta de VIH. En consulta 148/448 (33%) de los pacientes presentaba una carga viral detectable. Las variables que se asociaron a no tener una carga viral indetectable fueron: el sinhogarismo, practica de chemsex y no estar en TARV cuando se consigue llegar a la consulta de VIH. La mitad de los pacientes fueron contactados a los 6 meses de la primera valoración: 235 (99,6%) continuaba en TARV, 231 (98%) presentaba una carga viral plasmática indetectable para el VIH, 143 personas (61%) consiguieron reconocimiento de su derecho a asistencia sanitaria y 116 (50%) consiguieron trabajo.
Conclusiones: Los migrantes con infección por VIH que se encuentran en situación irregular son predominantemente varones jóvenes, de origen latinoamericano y con estudios superiores. A su llegada mantienen conductas sexuales de riesgo y presentan barreras para acceder al sistema sanitario, que dificultan el acceso al tratamiento antirretroviral. A pesar de utilizar circuitos de derivación directos, un tercio de las personas que son valoradas en consultas presentan carga viral del VIH detectable.

Sesión Póster Oral 4 – Pósteres Orales Básicos – 29 de noviembre – 15:00-16:45h

PO-31. ASOCIACIÓN DEL PERFIL DE EXPRESIÓN GÉNICA CON LA EVOLUCIÓN DE LA ENFERMEDAD HEPÁTICA TRAS EL TRATAMIENTO ANTIVIRAL EN PACIENTES COINFECTADOS CON VIH/VHC

A. Virseda Berdices[1], O. Brochado Kith[1], J. Berenguer[2], J. González García[3], C. Díez[2], V. Hontañon[3], T. Aldámiz Echevarría[2], R. Micán[3], C. Fanciulli[2], C. Busca[3], S. Resino[1], A. Fernández Rodríguez[1] y M.Á. Jiménez Sousa[1]

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Introducción y objetivos: La erradicación del VHC con tratamiento antiviral en pacientes coinfectados VIH/VHC reduce la morbilidad y mortalidad hepática y no hepática. Sin embargo, un subgrupo de pacientes continúa en riesgo de progresión de la cirrosis y desarrollo de carcinoma hepatocelular a pesar de la erradicación del VHC. Para entender mejor la patogenia de la progresión de la enfermedad hepática tras la erradicación del VHC hemos determinado el perfil de expresión génica en pacientes coinfectados VIH/VHC antes de iniciar tratamiento anti-VHC y estudiado su asociación con la evolución de la hepatopatía.
Métodos: Se realizó un estudio longitudinal prospectivo en 55 pacientes coinfectados VIH/VHC que fueron evaluados antes de la terapia antiviral para el VHC y 36/48 semanas tras alcanzar la respuesta virológica sostenida (RVS) (34 de ellos tratados con antivirales de acción directa (AADs) y 21 con terapia basada en interferón). A nivel basal, se secuenció masivamente el ARN mensajero (ARNm) de las células mononucleares de sangre periférica (CMSP). Se utilizó un modelo lineal generalizado con distribución binomial negativa ajustado por las variables significativas para identificar los genes expresados diferencialmente (DEG) entre pacientes que disminuyeron el valor de la rigidez hepática (LSM) estimada por elastografía, en más del 50% (LSM50) y aquellos que no lograron tal reducción tras la RVS (*fold change* (FC > 2 y q-valor < 0,05). Posteriormente, se realizó un análisis discriminante de mínimos cuadrados parciales (PLS-DA) con los DEG y se obtuvo el área bajo la curva característica operativa del receptor (AUROC).
Resultados: De los 55 pacientes de este estudio, 8 de ellos alcanzaron LSM50 (14,5%). La mediana de edad del grupo LSM50 fue de 47 años, siendo significativamente diferente al otro grupo de estudio (52 años). En el análisis de RNAseq se identificaron un total de 14.888 genes informativos. De ellos, se observaron 22 DEG que se asociaron significativamente con la disminución del LSM50. El PLS-DA mostró que estos 22 DEG discriminaban colectivamente a los pacientes LSM50 y los que no, con un AUROC de 0,87 (p < 0,001). Los genes que presentaron una mayor sobreexpresión fueron *SLC4A1* (LFC = 5,09), *ALAS2* (LFC = 5,95), *HBA1* (LFC = 4,89) y *HBD* (LFC = 4,35), estando *HBA1* y *SLC4A1* implicados en rutas relacionadas con el intercambio de gases en eritrocitos.
Conclusiones: El estudio del perfil de expresión génica en CMSP puede ayudar a explicar y predecir la progresión de la fibrosis hepática en pacientes coinfectados por VIH/VHC tras la RVS.

PO-32. CD4/CD8 RATIO ≥ 0.5 IS A RISK FACTOR OF ACUTE REJECTION IN HIV-INFECTED LT RECIPIENTS

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Introduction: HIV-infected liver transplant (LT) recipients have higher rates of acute rejection than uninfected recipients. Previously we identified host and donor genetic markers (HLA class I and II mismatches and interferon-λ3 and –λ4 gene polymorphisms) that can increase the risk of organ-rejection in HCV/HIV LT recipients. However, HIV-related factors of acute rejection have been poorly studied. We investigated whether virological and immunological status and type of antiretroviral therapy influence acute-rejection risk in HIV-infected LT recipients.
Methods: 272 consecutive HIV-infected patients undergoing LT from 2002-2012, then followed until December 2019, in 22 Spanish medical centers were included. All acute-rejection episodes were biopsy-proven. Acute-rejection prognostic-factor analysis was done using Cox proportional hazards model. Statistical analysis was done in SPSS 24.0.
Results: Median (IQR) age was 46 years (42-49); 78% of patients were male. Former IV drug use (74%) was the most frequent HIV risk factor. The etiology of end-stage liver disease was co-infection with HCV (80%), HBV (5%), HCV/HBV (11%) and non-viral etiology (4%). 20% of cases were cured of HCV pre-LT. Hepatocellular carcinoma was diagnosed in 27% of cases. At pre-LT, median (IQR) MELD was 15 (11;20) and CD4+T cell count was 277 (176;414) cells/mm^3. CD4/CD8 ratio was ≥ 0.5 in 77% of cases. 93% of patients had suppressed HIV viremia (VL < 200 copies/mL) on ART. Median (IQR) donor risk index was 1.6 (1.3; 1.9) and 35% of donors were ≥ 60 years. Initial immunosuppression was cyclosporin– and tacrolimus-based in 30% and 58% of cases, respectively. Post-LT ART was started after a median (IQR) of 7 (4;16) days and was based on raltegravir in 22% of cases. 72 (26%) recipients developed an acute rejection episode within the first 48 weeks post-LT. Median (IQR) time to acute rejection was 13.0 (10.0; 25.0) days. Donor and recipient age, pre-LT CD4/CD8 ratio ≥ 0.5, time to restart ART post-LT and RAL-based ART were independently associated with acute rejection. Patients with CD4/CD8 ratio ≥ 0.5 had > 3 times greater acute-rejection risk. This variable was also identified when focusing analysis only on HCV/HIV LT recipients (HR [95%CI] 5.02 [1.53; 16.52]).
Conclusions: Three HIV-infection related factors, namely CD4/CD8 ratio, time to restart ART post-LT and raltegravir-based ART are associated with acute rejection. These findings may help improve post-LT management in HIV-infected recipients.

PO-33. DASATINIB MODULATES ESSENTIAL METABOLIC PATHWAYS TO TACKLE HIV RESERVOIR IN CD4+ T CELLS WITHOUT AFFECTING CD8 AND NK CELLS

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Introduction and objectives: HIV infection is associated with increased immunometabolic demand in the infected cell that is coun-

terbalanced via hyperactive glycolysis and oxidative phosphorylation. Therefore, HIV selectively infects highly metabolic CD4+ T cells, being CD4+ TEM and TEMRA subpopulations, which are essential for the reservoir replenishment, those that show the highest metabolic activity in comparison with *naïve* and TCM. HIV-induced metabolic reprogramming cannot be completely restored by ART and may contribute to chronic inflammation and comorbidities in virally suppressed PLWH. Dasatinib is a potent cytostatic drug that interferes with HIV infection in CD4 and macrophages. Our aim was to determine if dasatinib may reduce the metabolic activity in viable CD4+ T cells to interfere with the formation and maintenance of HIV reservoir without affecting other essential cells.

Methods: CD4+ T cells isolated from healthy donors were activated with PHA/IL-2 for 72h with or without dasatinib 75 nM. PLWH on ART and dasatinib were also recruited. Phosphoproteome was analyzed by LC-MS/MS on Orbitrap. The synthesis of mitochondrial ATP was evaluated every 24h by chemiluminescence and the culture medium pH was also measured. The uptake of fluorescent glucose analog 2-NBDG, the expression of GLUT-1, the distribution of T-cell memory subpopulations, and T-cell viability were determined by flow cytometry.

Results: 1) Dasatinib deregulated the phosphorylation of more than 130 proteins involved in metabolic pathways such as glycolysis/glyconeogenesis, pyruvate metabolism, pentose phosphate pathway, inositol phosphate metabolism, phosphatidylinositol signaling system, glucagon signaling pathway, purine metabolism, and biosynthesis of amino acids. 2) Dasatinib reduced 2.1-fold (p = 0.0112) the synthesis of mitochondrial ATP in viable CD4+ T cells in comparison with cells treated with PHA/IL-2, which correlated with a reduced susceptibility to HIV infection. 3) Culture medium pH remained stable at 7.6 in the presence of dasatinib after 72h of activation but diminished to 7.2 without dasatinib. 4) Dasatinib interfered with the expression of GLUT1 and the glucose uptake induced by PHA/IL2 in all CD4+ T cell memory subpopulations: TN, TCM, TEM, and TEMRA, whereas NK and CD8+ T cells were unaffected and remained metabolically active (Fig.). 5) PLWH on treatment with ART and dasatinib showed reduced CD4+ TEM and TEMRA subpopulations, in accordance with the decreased metabolic activity in these cells.

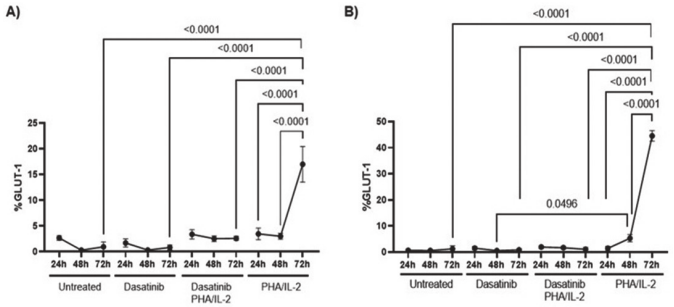

Figure1. Dasatinib significantly reduced the surface3 expression of glucose transporter 1 (GLUT1) induced by PHA/Il2 in CD4+ TEM (A) and TEMRA (B) cells, the major contributors to HIV reservoir replenishment.

Conclusions: Treatment with dasatinib selectively relegated viable CD4+ cells to a resting state in which glycolysis and mitochondrial ATP synthesis were stalled, impeding both HIV infection and reservoir reactivation and replenishment, whereas CD8 and NK cells remained unaffected.

PO-34. DASATINIB PROTECTS MONOCYTE-DERIVED MACROPHAGES FROM HIV INFECTION AND ENHANCES THEIR MOBILITY AND PHAGOCYTIC POTENTIAL

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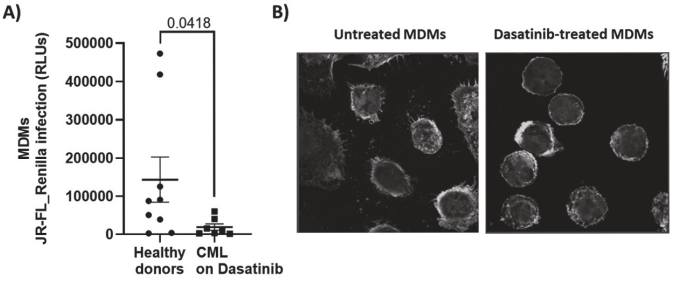
Introduction: Macrophages are significant mediators of inflammatory comorbidities in PLWH. As infection progresses, HIV is increasingly macrophage-tropic and, as CD4 are depleted, macrophages become the main source of viremia. Dasatinib is a cytostatic drug that efficiently interferes with HIV infection in CD4+ T cells. The main objective of this study was to evaluate if dasatinib may also interfere with HIV infection of macrophages without affecting their functionality as major mediators of innate immunity.

Methods: CD14+ cells isolated from PBMCs of healthy donors (n = 9) and individuals with chronic myeloid leukemia (CML) on treatment with dasatinib (n = 7) were differentiated to monocyte-derived macrophages (MDMs) for 5 days and then infected with JR_FL_Renilla for 48h. HIV-1 infection was analyzed by flow cytometry (antibody against HIV p24, clone kc57). Cytoskeleton structure was analyzed after staining tubulin and phalloiding using confocal multispectral system Leica Stellaris. MDMs itineraries and phagocytic capacity in the presence of fluorescent *Candida albicans* (1:1) were analyzed with Leica Thunder Imager system. Cell internal structures were analyzed with non-invasive, label-free, 3D, high-resolution Nanolive's CX imaging platform.

Results: 1) HIV infection was reduced 7.5-fold (p = 0.0418) in MDMs isolated from individuals on treatment with dasatinib, in comparison with healthy donors (Fig. 1A). 2) Tubulin and phalloidin staining of MDMs treated with dasatinib showed a rounded morphology without visible filopodia, while untreated MDMs had numerous filopodia (Fig. 1B). 3) In vivo analysis showed that the addition of *C. albicans* to MDMs induced mobility trajectories 2.3-fold wider when MDMs were treated with dasatinib in comparison with untreated cells. Phagocytic capacity was also increased 1.2-fold in dasatinib-treated MDMs. 4) *In vivo* 3D observation of yeast phagocytosis showed that dasatinib-treated MDMs contained higher quantity of intracellular vesicles.



Conclusions: Dasatinib protected MDMs from HIV infection and induced a rounded morphology without visible attachments to the surface. Moreover, dasatinib-treated MDMs showed higher mobility than cells from healthy donors, with broader movements that follow linear pathways, and higher phagocytic capacity. Therefore, the phenotypic changes induced by treatment with dasatinib did not affect the role of macrophages as phagocytes and antigen-presenting cells.

PO-35. EXTRACELLULAR VESICLES AS POTENTIAL MECHANISM OF CHRONIC INFLAMMATION IN HIV PATIENTS

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Introduction: Increased systemic inflammation, associated with different morbidities, has emerged as a main problem in the clinical management of HIV-infected patients. Extracellular vesicles (EVs) carrying HIV elements and host pro-inflammatory molecules have been recently proposed as a potential mechanism contributing to this inflammatory state. Herein, we have analyzed several molecules associated to systemic inflammation, endothelial activation and coagulation in plasma-derived EVs from two groups of HIV patients with controlled HIV replication (spontaneously or by cART) and in a group of non-controller patients with replicating HIV.
Methods: Thirty HIV patients were included: 10 elite controllers (EC), 10 cART-suppressed (NC-TT) and 10 cART-*naïve* with high levels of HIV plasma viremia (NC-NT). Ten uninfected volunteers (UC) were also included as reference group. Plasma EVs were isolated by Size Exclusion Chromatography and lysed with triton X100 to release its content. Levels of fourteen different parameters related to systemic inflammation, endothelial activation and coagulation were evaluated using a Bio-Plex 200 System-Biorad and a customized kit of Procarta-Plex. Inter-group differences and potential associations were tested by non-parametric tests.
Results: Among the different markers analyzed, the endothelial activation marker ICAM1 (intercellular cell adhesion molecule 1) and the coagulation marker PAI-1 (plasminogen activator inhibitor 1) were differentially expressed between the study groups. HIV^+ patients showed increased levels of ICAM1 and PAI-1 compared to HIV^- UC volunteers (ICAM1: 8,869 [6,780-12,645] *vs.* 6,620 [5,877-7,101] pg/mL, p = 0.006; PAI-1: 45 [29-75] *vs.* 32 [21-44] pg/mL, p = 0.054). Compared to UC volunteers, both NC-NT (p = 0.011) and NC-TT (p = 0.001) patients presented the highest levels of ICAM1 (11,841 [7,807-15,260] and 8,970 [6,998-10,624] pg/mL in NC-NT and NC-TT respectively). In contrast, PAI-1 levels in NC-NT patients were similar to those of UC volunteers but were increased in patients with controlled viral replication, especially in NC-TT group (71 [25-106] *vs.* 32 [21-44] pg/mL in NC-TT and UC respectively, p = 0.029).
Conclusions: Our results show the existence of increased levels of endothelial activation and coagulation markers carried by EVs in the setting of HIV infection. This phenomenon was observed in both uncontrolled and controlled viral replication, supporting an important role of EVs as mediators in the HIV-associated persistent inflammatory state despite the control of viral replication.

PO-36. EXCEPTIONAL HIV-1 POST-TREATMENT CONTROL ASSOCIATED WITH STRONG NK AND ΓΔ CYTOTOXIC T-CELLS: A CASE REPORT

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Introduction: Although ART is effective in suppressing viral replication, HIV persists in reservoirs and rebounds after stopping therapy. However, there are few patients, such as post-treatment controllers (PTC), who are able to maintain viral loads below detection limits without ART, being a realistic model for the HIV-functional-cure. We describe the mechanisms of control of an exceptional PTC (> 15 years).
Methods: A 59-year woman with sexually-acquired acute HIV-infection was included in the `Immune-mediated PHI trial´ (NCT00979706), involving several interventions: short course of low doses of CsA, IL-2, GM-CSF and Peg-α-IFN followed by analytical STI. Virological studies were performed: total and integrated HIV-1 DNA in $CD4^+$ T cells and rectal tissue, viral outgrowth assay (qVOA), HIV-1 infectivity in PBMC and $CD4^+$ T cells cultures and viral inhibitory activity (VIA) of autologous $CD4^+$T cells with NK and $CD8^+$ T cells. NK and T cell phenotype was determined by flow-cytometry. HLA class I, δ32CCR5 and NKG2C alleles were genotyped.
Results: After antiretroviral and immunomodulatory treatment, the patient maintained undetectable viral load in plasma for 15 years. HIV-1 subtype was CFR_02AG, R5-tropic. We found a pronounced and progressive fall of the viral reservoir (VR): total HIV-DNA (from 4,573.50 to 95.33 copies/10^6 $CD4^+$T cells) and integrated proviral DNA (from 85.37 to 5.25 copies/10^6 $CD4^+$T cells).VR in rectal biopsy was 3 HIV DNA total copies/10^6 cells and qVOA detected 1.61 UIMP at year 9. VIA assay showed strong inhibition of *in vitro* replication in co-cultures with autologous NK-cells or $CD8^+$T cells at 1:2 ratio (75% and 62%, respectively). Co-cultures with NK and $CD8^+$ T cells resulted in 93% inhibition of HIV-replication. Higher levels of both $NKG2C^+$-memory-like NK cells and $NKG2C^+\gamma\delta^+$ T cells than referenced data from untreated normal HIV-infected progressors were detected (46.2 *versus* 24.0% and 64.9 *versus* 19.7%, respectively). In fact, we found that the expansion over the clinical course of these subpopulations from the PTC woman, inversely correlated with the amount of integrated proviral HIV-DNA (p < 0.05). The patient has A*29:01/A*29:01, B*44:03/B*44:03, C*16:01/C*16:01 HLA-I, wt/wt CCR5 and wt/wt NKG2C alleles.
Conclusions: We describe the case of functional cure in a 59-years-old woman treated during PHI that has maintained undetectable viral load for 15 years without ART. Replication-competent HIV-1 could be isolated by qVOA. $NKG2C^+$-memory-like NK cells and $\gamma\delta^+CD8^+$ T cells could contribute to the control of viral-replication and functional-cure observed. Strategies able to expand these cells could help to achieve HIV-functional-cure.

PO-37. LOWER T-CELL RESPONSES AGAINST SARS-COV-2 VARIANTS OF CONCERN AFTER MRNA VACCINATION AND RISK OF BREAKTHROUGH INFECTIONS IN PEOPLE LIVING WITH HIV

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Introduction: SARS-CoV-2 variant of concern (VOC) B.1.1.529 (Omicron) presents a surprisingly large number of mutations in its spike protein escaping from antibody neutralization. Thus, it is important to determine how well T-cell responses perform against different variants including Omicron in people living with HIV (PLH) following COVID-19 vaccination and the impact on new infections during follow up.
Methods: Prospective cohort study of PLH who underwent blood tests for humoral and cellular response after two doses an mRNA vaccine against SARS-CoV-2. Humoral (anti-S IgG, CLIA, Abbott; binding antibody units (BAU)/ml) and IFN-γ producing T cell responses to spike peptides of the ancestral virus, and Delta and Omicron variants were analysed.
Results: Overall, 142 PLH were included. Median age was 53 years (range, 24-78), 83% were male, and 41% had at least one comorbidity. Median nadir CD4+ count was 273/mm³, and 26% of the individuals had a previous AIDS diagnosis. Currently, median CD4+ count was 659/mmc and HIV RNA viral load was below 50 copies/ml in 99% of the individuals. After a median time of 53 days from the second vaccine dose, humoral responses were observed in 96% of cases (median 834 BAU/mL; interquartile range, IQR, 169-1871). Humoral and T-cell

responses to original SARS-CoV-2 were highly correlated (rho = 0.657; p < 0.01). In addition, there was a high correlation between T-cell responses to the original strain, Delta, and Omicron variants. However, CD4+ and CD8+ T-cell responses were significantly lower to Delta in proportion (83% and 82% against Delta variant, 72% and 74% against Omicron variant, respectively), and in magnitude (3% and –20% for Delta, –33% and –28% for Omicron variant). A total of 29 (17%) breakthrough infections were observed during a median follow-up of 351 days, associated with a lower level of specific antibodies (890.8 *vs.* 1559.7 BAU/mL; p = 0.027), and with a lower magnitude of CD4+ and CD8+ T cell responses to the different variants (statistically significant for CD8+ T-cell response).
Conclusions: T-cell responses against Delta and Omicron spike peptides, although preserved in nearly two thirds of PLH, were significantly lower than to the original strain after two doses of an mRNA vaccine. Importantly, this lower response was associated with breakthrough infections during follow-up.

PO-38. NON-SPECIFIC NEUTRALIZATION AGAINST SARS-COV-2 IN SAMPLES FROM HIV-INFECTED INDIVIDUALS IS ASSOCIATED TO INTEGRASE INHIBITORS TREATMENT

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Introduction: The presence of neutralizing antibodies (NAbs) is a major correlate of protection for several viruses including SARS-CoV-2. Different *in vitro* pseudoviruses-based assays to detect SARS-CoV-2 NAbs have been described. However, the determination of specific NAbs against SARS-CoV-2 in HIV-infected individuals could be influenced by treatment or cross-neutralization activity when using HIV-pseudoparticles. Here, we compare two assays using HIV or VSV-based particles pseudotyped with SARS-CoV-2 spike to address this issue.
Methods: We evaluated blood plasma/sera from HIV-infected individuals who had been infected (COVID-19 recovered) or not (COVID-19 *naïve*) by SARS-CoV-2. Neutralization assays with serial dilutions of heat-inactivated plasma/sera (56 ºC for 30 minutes) or purified IgG were performed, which were pre-incubated with titrated pseudoviruses (1h at 37 ºC) and plated with VeroE6-cells. 24-48h post-infection cells were lysed and viral infectivity was assessed by measuring luciferase activity. HIV-pseudoviruses were prepared by co-transfection of HEK-293T cells with SARS-CoV-2 spike protein and NL4-3δenv-Ren backbone (HIV-SARS-CoV-2); and VSV-pseudoviruses, by transfection of HEK-293T with SARS-CoV-2 spike protein followed by infection with G*δG-VSV-Luc virus (VSV-SARS-CoV-2). Sigmoid curves and NT50 (neutralizing titer 50) were calculated by non-linear regression and comparative analyses were performed with the Wilcoxon test.
Results: A high proportion of COVID-19 *naïve* individuals (67%) displayed neutralization activity against SARS-CoV-2 (NT50 > 32) when an HIV-pseudovirus assay (HIV-SARS-CoV-2) was used, with a NT50 median of 632 (IQR: 16-1535). However, we did not observe neutralization activity against VSV-SARS-CoV-2 in any of these individuals. In COVID-19 recovered individuals, we observed neutralization activity against HIV-SARS-CoV-2 in all samples, with a NT50 median of 1,550 (IQR: 492-3,388). However, only 75% of individuals showed neutralization activity when a model based on VSV-SARS-CoV-2 pseudotypes was used (NT50 median of 100.5 [IQR: 20-1,353]). Moreover, we observed that non-specific neutralization of HIV-SARS-CoV-2 on HIV-infected individuals was associated with integrase inhibitors treatment (p < 0.01), indicating that these drugs could block integration of the lentiviral vector and impair luminescence activity lading to false positive neutralization results. This effect was overcome by IgG purification, which cleans the drugs in sera/plasma, obtaining a strong positive correlation between both assays (r = 0.88; p < 0.0001).
Conclusions: The VSV-based pseudovirus is able to determine anti-SARS-CoV-2 neutralizing activity with a higher specificity compared to the HIV-SARS-CoV-2 system in HIV-infected individuals. Purification of IgG reduced the non-specific neutralization activity caused by ART on HIV-based pseudovirus, allowing more specific anti-SARS-CoV-2 responses. In summary, our study proposed methodological alternatives based on pseudoviruses to determine specific humoral responses against SARS-CoV-2 in HIV-infected individuals.

PO-39 MARACOVID: A TWO-CENTER, RANDOMIZED, OPEN-LABEL, CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND TOLERABILITY OF MARAVIROC IN ADULT PATIENTS HOSPITALIZED WITH MILD TO MODERATE COVID-19 PNEUMONIA

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Introduction: Severe respiratory progression of COVID-19 pneumonia involves a prominent role in the innate immune response. Detrimental effects of C5a, studied in experimental models, are partly mediated through C-C chemokine receptor type 5 (CCR5) activation. Maraviroc (MVC) is a CCR5 inhibitor used to treat HIV infection. Whether the use of MVC in hospitalized patients with non-severe COVID-19 pneumonia prevents progression is uncertain.
Methods: We conducted a phase 2, randomized, open-label trial to evaluate the efficacy and safety of maraviroc in the prevention of severe acute respiratory distress syndrome (ARDS) development in hospitalized patients with mild-to-moderate COVID-19 pneumonia. Enrolment was carried out from July 2020 through January 2021, at two hospitals in Spain. Patients were randomized in a 1:1 ratio to receive a 14-day course of maraviroc (MVC) plus standard of care (SOC), or SOC alone. MVC was dosed orally at 300 mg twice a day. The primary endpoint was to evaluate the proportion of patients developing severe ARDS during the 28 days of follow-up. Secondary outcomes included all-cause mortality, time to clinical improvement; disease progression analysis measured by different ventilatory, clinical, or therapeutic parameters, and safety analysis.
Results: On January 2021, the results of a planned interim analysis recommended stopping enrollment for futility after 60 patients (30 in the MVC group and 30 in the SOC group) had been randomized. The primary analysis was performed on the per-protocol population including 27 patients in the experimental arm and 29 in the control group. The median age was 55 years (IQR 45-67); 31 (55.4%) were males, and 29 (51.8%) were of Latin ethnicity. The most common comorbidity was hypertension. Only four patients met severe ARDS criteria, 2 in each arm, so no significant difference was found in the primary endpoint. We also found no differences in secondary endpoints either, including 28-day mortality (1 [3.7%] died in the intervention group *vs.* 0% in the SOC group), time to clinical improvement, the requirement of high flow equipment or support treatments, and the clinical progression as measured by an ordinal 7-point scale. Additionally, no differences in inflammatory markers levels (ferritin, IL-6, procalcitonin) were found at 3, 5, 7, or 14 days after randomization. There were no significant differences in SAE reports neither among all non-serious AEs.
Conclusions: Our results do not suggest a beneficial effect of maraviroc on hospitalized patients with mild to moderate COVID-19 pneumonia.