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XIII Congreso Nacional GeSIDA

Sitges, 27-30 de noviembre de 2022

Sesión de Comunicaciones Orales 1
28 de noviembre – 10:15-12:05h

CO-01. DERIVADOS DE LA MICROBIOTA COMO ALTERNATIVA AL CRIBADO ACTUAL DE DISPLASIA ANAL

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Introducción: El riesgo de cáncer anal está aumentado en personas con VIH, especialmente en HSH, que presentan cambios en la microbiota que podrían explicar el mayor potencial oncogénico del VPH. La baja especificidad de la actual estrategia de cribado de lesiones escamosas intraepiteliales de alto grado (HSIL) dificulta la prevención del cáncer anal. Investigamos en cepillados anales marcadores de HSIL asociados a la microbiota.

Métodos: Incluimos una cohorte de derivación y otra de validación en 4 centros clínicos de España e Italia. Los participantes en el estudio fueron HSH en cribado de HSIL que incluía anoscopia de alta resolución y biopsias anales. Extrajimos el ADN bacteriano, las proteínas y los metabolitos de las muestras anales, donde realizamos secuenciación del gen16SrRNA, espectrometría de masas y cuantificación dirigida de metabolitos.

Resultados: De 213 participantes, la cohorte de derivación incluyó 167 pacientes con 70 casos de HSIL y la cohorte de validación incluyó 46 pacientes con 25 casos de HSIL. Los pacientes con HSIL mostraron una mayor abundancia de *Prevotella copri*, mientras que la de *Streptococcus periodonticum* y *Sneathia sanguinegens* fue menor.

Las bacterias asociadas a HSIL sobreexpresaban proteínas que convergían en la producción de succinil-CoA y cobalamina, cuyos niveles fueron significativamente superiores en los sujetos con HSIL. La combinación de succinil-CoA y cobalamina superó a la citología anal, mejorando la sensibilidad del 91,2% al 96,6%, la especificidad del 34,1% al 81,8%, el valor predictivo positivo del 48,1% al 77,8% y el valor predictivo negativo del 85,3% al 97,3%. Mientras que la citología anal solo clasificó correctamente al 59,9% de los pacientes, la combinación de ambos biomarcadores mejoró la clasificación hasta el 87,7%. Esta prueba superó la validación interna (AUC ajustado 0,877) y externa. De 98 resultados citológicos falsos positivos, la prueba metabólica reclasificó a resultados verdaderos negativos 49 (81,9%). Por último, demostramos una mayor producción in vitro de succinil-CoA y cobalamina de *Prevotella copri* –aumentada en participantes con HSIL– frente a *Sneathia sanguinegens* –disminuida en los pacientes con HSIL-.

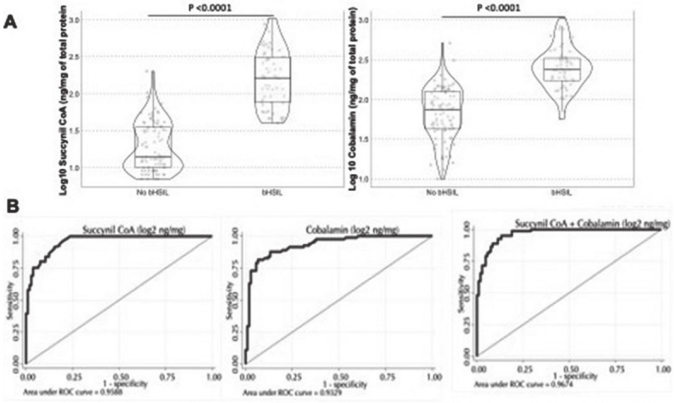

Figura 1A. Concentración de succinil-CoA, en pacientes con HSIL vs. sin HSIL en la cohorte de derivación.
Figura 1B. Área bajo la curva ROC estimada mediante regresión logística considerando HSIL confirmada el desenlace y como predictores la succinil-CoA, la cobalamina, o ambos marcadores en combinación.

Conclusiones: La cobalamina y el succinil-CoA están sobreexpresados en la microbiota anal de las personas con HSIL y muestran una excelente capacidad diagnóstica. La combinación de ambos metabolitos supera a la prueba de referencia, la citología anal, para discriminar a los pacientes con HSIL. Por tanto, hemos descubierto dos potentes biomarcadores, para los que se pueden establecer fácilmente métodos de detección que podrían mejorar la estrategia actual de cribado del cáncer anal.

CO-02. LIMITED HUMORAL AND SPECIFIC T-CELL RESPONSES AFTER SARS-COV-2 VACCINATION IN PLWH WITH POOR IMMUNE RECONSTITUTION

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Introduction: The coronavirus disease 2019 (COVID-19) pandemic has caused significant morbidity and mortality and stressed healthcare systems worldwide. Successful development of safe and effective vaccines against COVID-19 has mitigated the impact of this disease. However, vaccine-responsiveness in people living with HIV-1 (PLWH) with poor immune reconstitution is not yet well characterized. We analyzed humoral and cellular immune responses induced by SARS-CoV-2 mRNA vaccines in people living with HIV-1 (PLWH) with < 200 $CD4^+$ T-cells.
Methods: Prospective cohort study including 58 PLWH with $CD4^+$ T-cell counts < 200 cells/mm^3 within the last 6 months, 36 with $CD4^+$ T-cell counts > 500, and 33 HIV-1-negative controls. Participants received 2 doses of COVID-19 mRNA vaccines (BNT162b2 or mRNA-1273). Antibodies against the SARS-CoV-2 Spike protein (anti-S IgG) and the receptor-binding domain (anti-RBD IgG) were quantified before and four weeks after the first and the second dose of BNT162b2 or mRNA-1273. Viral neutralization activity and T-cell responses four weeks after the second dose (w8) were also determined in a subgroup of individuals.
Results: Median (IQR) CD4+ T cell count at baseline was 173 (117; 257) cells/mm^3 and 785 (655; 966) cells/mm^3 in the HIV < 200 and HIV > 500 groups, respectively. Proportion of individuals virologically ART-suppressed at the moment of vaccination was 81% and 100% respectively (p = 0.0058). At w8, anti-S/anti-RBD IgG responses increased in all groups (p < 0.0001). However, individuals in HIV < 200 group had a significantly weaker response; median (IQR) S-IgG and RBD-IgG at w8 were 153.6 (26.4; 654.9) and 171.9 (61.8; 425.8) in the HIV < 200 group compared to 245.6 (145; 824) and 555.8 (166.4; 1751) in the HIV > 500 group, and 274.7 (193.7; 680.4) and 281.6 (181; 831.8) BAU/mL in controls (p < 0.05). Neutralizing capacity and specific T-cell immune responses were absent or reduced in 33% of the HIV < 200 group, compared with 3.7% in the HIV > 500 (p = 0.0003).
Conclusions: One third of PLWH with CD4+ T-cell counts < 200 cells/mm^3 show low anti-S/anti-RBD IgG levels, reduced in vitro neutralization activity against SARS-CoV-2 and no vaccine-induced T-cells after receiving COVID-19 mRNA vaccines.

CO-03. HIV TESTING TRAINING FOR NON-HIV-SPECIALISTS IN A TERTIARY HOSPITAL: CHANGE IN ATTITUDES AND RATES OF HIV SCREENING

A. García Ruiz de Morales, J. Martínez Sanz, M.J. Vivancos, C. Cano, M. Sánchez Conde, B. Romero, M. Vélez-Díaz-Pallarés, M.D. González Vázquez, F. Gea, J.C. Galán and M.J. Pérez Elías

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Introduction: National and international HIV testing guidelines are poorly known by non-HIV specialists. Increasing awareness is essential to improve HIV screening. Few programs targeting these groups have been reported.
Methods: In a tertiary hospital, six infectious diseases physicians provided a 1-hour personalized training session on HIV screening to other departments. A brief questionnaire was used before and after training to evaluate attitudes towards HIV screening. We compared the absolute number of tests requested, the screening rate per 1,000 patients attended, and new HIV diagnoses in the 6-month period before and after training, for each department.
Results: From March to November 2019, a total of 346 non-HIV-specialists (90% < 55 years,59% female), from 31 hospital departments (17 medical,14 surgical), were trained and answered the questionnaire. According to pre-training questionnaire, 20% of non-HIV specialists (28% medical *vs.* 8% surgical, p < 0.001) were aware of HIV testing guidelines (5% ordered routinely, 60% with any obvious exposure risk /indicator conditions, and 35% never did so). In post-training responses, 98% considered the training useful, and responses showing a positive attitude towards routine HIV testing increased to 20%, while those who never requested tests decreased to 2% (p < 0.001). Out of an estimated number of 785,499 patients attended in both periods, we observed a 24% increase in HIV tests requested (p < 0.001), significant in medical and surgical services; this increase was driven by six medical and one surgical department (Table). An increase in new HIV diagnoses in the post-training period (25 *vs.* 37) was also seen, although only in medical departments (19 *vs.* 32; p = 0.068).
Conclusions: Non-HIV-specialists reported poor knowledge of HIV screening, being worse in surgical departments. Directed training was considered useful and significantly improved some attitudes towards HIV testing. We observed an increase in HIV testing coverage and its effectiveness, with marked differences between departments.

CO-04. EVALUATION OF DORAVIRINE/LAMIVUDINE/TENOFOVIR DISOPROXIL FUMARATE FOR NON-OCCUPATIONAL POST EXPOSURE PROPHYLAXIS, A PROSPECTIVE OPEN-LABEL STUDY (DORAVIPEP)

A. Inciarte Portillo, A. Ugarte, M. Martínez-Rebollar, B. Torres, E. Fernández, M. Laguno, J. Ambrosioni,, D. Agüero, I. Chivite, L. Berrocal, A. Foncillas, A. González-Cordón, P. Puerta, L. de la Mora, E. de Lazzari, S. Herrera, N. García-Pouton, J. Calvo, M. Hernández Meneses, P. Monzo, A. Rodrigo, P. Callau, L. Barrero, E. Solbes, E. Martínez, J.L. Blanco, J. Miró and J. Mallolas

Hospital Clínic de Barcelona, Barcelona.

Introduction: Most guidelines still recommend multiple pill regimens for post-exposure prophylaxis (PEP), and completion rates for PEP are often low. Few studies assess safety, tolerability, and adherence to new single table regimens (STR). We evaluated the combination of Doravirine/Lamivudine/Tenofovir as STR for non-occupational

CO-03. Tabla

Departments	HIV tests/10^3 attended patients		p	HIV Diagnoses/10^5 attended patients		p
	Before Training	After Training		Before Training	After Training	
All Medical & Surgical	6.7	8.3	< 0.001	3.2	4.7	0.13
All Medical Dept.	6.0	7.1	< 0.001	4.2	7.0	0.07
Emergency room	5.2	6.6	0.014	7.8	17.8	0.16
Gastroenterology	7.6	9.3	< 0.01	1.9	1.9	1
Endocrinology	7.3	9.6	< 0.01	10.2	17.0	0.48
Intensive care	54.3	135.8	< 0.001	0	0	-
Preventive Health	28.1	65.9	< 0.001	84.0	294.1	0.09
Nephrology	25.4	31.6	< 0.001	10.7	37.5	0.09
Surgical	7.5	8.7	< 0.001	1.8	1.5	0.76
Gynecology	45.2	62.1	< 0.001	2.4	1.2	0.31

PEP.

Methods: This is a prospective, open-label, single-arm study. Individuals attending the emergency room due to potential sexual exposure to HIV and who met the criteria for PEP received Doravirine/Lamivudine/Tenofovir. The primary endpoint was PEP non-completion on day 28, and the secondary endpoints were adverse effects, adherence, and rate of seroconversions. Follow-up consultations were appointed on days 10, 60, and 120. Clinical trials.gov number: NCT04233372.

Results: From 01-09-2020 to 14-03-2022, 399 individuals were enrolled in the study. The median age was 30 (27-36) years, and 91% (n = 365) were males. The mode of exposure was HSH in 84% (n = 331) and risk assessment as ascertained by the treating provider, was high in 97% (n = 385) of the cases. PEP users self-referred use of recreational drugs in 30% (n = 109) of cases. PEP non-completion at day 28 was 26% (n = 103) (95%CI: 22%; 30%), reasons for non-completion were: Loss to follow-up 92 (89%), Intolerance 9(9%) and Patients Decision/Withdrawal Consent 2 (2%). In the multivariate regression model, older age for a patient makes it less likely for him to discontinue the treatment prematurely 0.95 (0.92;0.98) p = 0.0016. Adverse events were reported by 70 (18%) patients during the treatment period. Gastrointestinal symptoms were the most common, 51% (n = 49), followed by neurological, 30% (n = 29). There were no potentially life-threatening (grade IV) adverse events. Most of the adverse events were mild and self-limiting, 83% (n = 82). Adherence to PEP in the assessed users was 96% (337/351) and 99% (285/289) by self-report and pill count data at day ten and week 4, respectively. There were no cases of HIV transmission in this cohort.

Conclusions: Doravirine/Lamivudine/Tenofovir is a well-tolerated option for once-daily PEP that compares favourably with other recommended PEP regimens.

CO-05. EPIDEMIOLOGICAL TRENDS OF HIV/HCV COINFECTION IN SPAIN, 2015-2021

C. Fanciulli[1], J. Berenguer[1], C. Busca[2], C. García[3], S. del Campo[4], A. Hernando[5], J. Vergas[6], P. Domingo[7], J. Navarro[8], J. Santos[9], L. Morano[10], J.A. Iribarren[11], J. Moreno[12], I. Santos[13], A. Artero[14], M.J. Galindo[15], S. Reus[16], M. Montero[17], A. Rivero-Román[18], C. Armiñanzas[19], A. Villoslada[20], O.L. Ferreiro[21], J.E. Losa[22], J. Sanz[23], C. Manzardo[24], B. de la Fuente[25], G. Gaspar[26], S. Veloso[27], L. Pérez[28], L. Force[29], E. Bernal[30], C. Rodríguez[31], D. Corps[32], A.J. Ortí[33], C. Martín[34], R. Teira[35], G. Alonso[36], V. Víctor[37], R. Silvariño[38], P. Geijo[39], C. Oliva[40], I. Jarrín[41] and J. González-García[2]

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Objectives: We assessed the prevalence of anti-hepatitis C virus (HCV) antibodies and active HCV infection (HCV-RNA-positive) in people with HIV (PWH) in Spain in 2021 and compared the results with those of five similar studies performed during 2015-2019.

Methods: The study was performed in 41 centers. The sample size was estimated for an accuracy of 0.75%. Patients were selected by random sampling with proportional allocation.

Results: The reference population in 2021 comprised 46,059 PWH, and the sample size was 1,421. HCV serostatus was known in 1,406 (98.9%), of whom 398 (28.3%) were HCV antibody (Ab)-positive (72.1% were prior injection drug users and 11.8% men having sex with men). Of these 398 PWH, 320 cleared HCV after anti-HCV therapy, 65 cleared HCV spontaneously, 12 were HCV-RNA-positive, and 1 had unknown HCV-RNA. The prevalence of HCV-RNA-positive was, therefore, 0.85% (95%CI 0.44-1.49). Of the 12 HCV-RNA-positive PWH, HCV was acquired within the previous 12 months in 2. Besides, 5 of these 12 patients were already on anti-HCV therapy or programmed to start it. Cirrhosis was present in 4.2% of PWH overall, 18.4% of those who cleared HCV after anti-HCV therapy, and 0% of HCV-RNA-positive PWH. A summary of the main findings in the six national cross-sectional studies is shown in the table.

Conclusions: In Spain, the prevalence of active HCV infection among PWH at the end of 2021 was 0.85%, i.e., 96.1% lower than in 2015. Increased exposure to DAAs was probably the main reason for this sharp reduction. Despite these advances toward the micro elimination of HCV in this population group, liver cirrhosis remains of concern among those who cured the infection with anti-HCV therapy.

CO-06. VIGILANCIA DE LA RESISTENCIA A ANTIRRETROVIRALES EN NUEVOS DIAGNÓSTICOS DE INFECCIÓN POR VIH-1 EN ESPAÑA (2020-2022)

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CO-05. Trends in HIV/HCV coinfection in Spain 2015-2021

	2015	2016	2017	2018	2019	2020	2021	p trend
Centers	41	43	43	43	41	-	41	
Reference population	35,791	38,904	40,322	40,650	41,976	-	46,059	
Sample size	1,867	1,588	1,690	1,733	1325	-	1421	
Tested for HCV Ab	98.71%	99.81%	99.11%	99.31%	99.32%	-	98.94%	
HCV Ab-positive	37.71%	34.57%	33.97%	33.59%	28.57%	-	28.31%	< 0.001
HCV-RNA-positive	22.06%	11.75%	8.00%	3.72%	2.21%	-	0.85%	< 0.001
Anti-HCV treatment uptake	59.3%	74.7%	82.4%	92.2%	95.0%	-	97.0%	< 0.001

Introducción y objetivos: La vigilancia de la resistencia a antirretrovirales (ARV) en infecciones por VIH-1 es esencial para definir la mejor estrategia en la selección de fármacos en tratamientos de primera línea y para evaluar la necesidad de realizar estudios genotípicos de resistencia en nuevos diagnósticos (ND). En este estudio analizamos las resistencias a ARV en ND de infección por VIH-1 en España en 2020-2022 y sus implicaciones en la elección de fármacos ARV.
Métodos: Las secuencias parciales de *pol* de 1.066 infecciones por VIH-1 diagnosticadas en 2020-2022 en 13 comunidades autónomas de España fueron analizadas mediante el programa HIVdb de la HIV Drug Resistance Database de la Universidad de Stanford para la determinación de resistencias a ARV. Los virus con potencial baja resistencia fueron considerados susceptibles. El subtipo y la pertenencia a clusters de transmisión (CT) se determinaron mediante análisis filogenéticos de máxima verosimilitud aproximada utilizando FastTree2. Designamos CT a las agrupaciones de ≥ 4 infecciones con un apoyo del nodo ≥ 0,95 de valor SH-*like*.
Resultados: La mayoría de los ND eran varones (88%), hombres que tienen sexo con hombres (58%), de origen español (52%) e infectados por virus de subtipo B (66%). De los 1.054 pacientes con secuencia de proteasa (PR)-retrotranscriptasa (RT), el 2,5% presentó resistencia a inhibidores de la proteasa, 3,6% a inhibidores nucleosídicos de la RT (INRT) y 14% a inhibidores no nucleosídicos de la RT (INNRT). En los 334 ND con secuencia de integrasa, se detectó una baja frecuencia (1,5%) de resistencia a inhibidores de integrasa (INI), siendo todos ellos susceptibles a INI de segunda generación. En 18 CT, de 4 a 40 individuos, se están transmitiendo virus resistentes a ARV, que representan el 21% de ND con resistencia. En 2 pacientes con fracaso en la profilaxis preexposición (PrEP) se detectó la mutación M184V de resistencia a INRT.
Conclusiones: La baja frecuencia de mutaciones de resistencia a INI apoya su uso en los tratamientos de primera línea de la infección por VIH-1. La alta prevalencia de resistencia a INNRT hace necesario el estudio genotípico antes de incluir estos ARV en el tratamiento, tal como sugieren las actuales guías terapéuticas. Recomendamos la vigilancia epidemiológica molecular continua del VIH-1 para monitorizar la resistencia a ARV, la aparición de mutaciones que puedan interferir con la eficacia de nuevos ARV o en la PrEP y detectar de forma temprana CT con resistencia a ARV, para limitar su expansión implementando medidas preventivas.

CO-07. MORTALITY DUE TO NON-AIDS DEFINING MALIGNANCIES IN ADULTS LIVING WITH HIV

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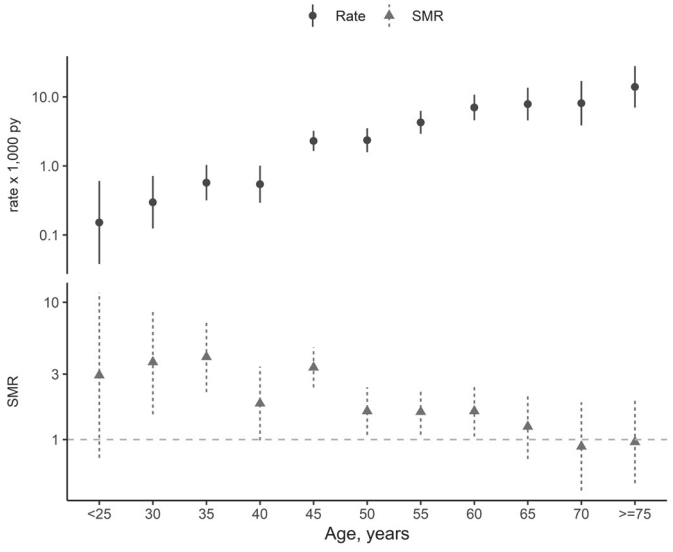
Objectives: To evaluate rate and prognostic factors of mortality due to non-AIDS defining malignancies (NADM) among HIV-positive individuals from the cohort of the Spanish AIDS Research Network (CoRIS) during 2004-2020.
Methods: We included antiretroviral-*naïve* individuals aged ≥ 20 years at enrolment, recruited between January 1, 2004, and December 31, 2020. We considered all deaths due to cancer, except those due to AIDS defining malignancies such as Kaposi sarcoma, certain types of non-Hodgkin lymphomas and cervical cancer. We estimated overall and cause-specific age-, sex– and period-adjusted mortality rates and standardised mortality ratios (SMRs) using NADM mortality rates from the Spanish general population. We applied cause-specific Cox proportional hazard models accounting for competing risk, with age as time-scale to identify factors associated with risk of death due to NADM.
Results: Of the 17,329 individuals included, 85% were men and median age was 35 years. The most frequent transmission route was homo/bisexual contact (62%). We identified 161 deaths due to NADMs over 104,773 person-years of follow-up, accounting for 20% of all deaths and yielding a mortality rate of 1.53 (95% confidence interval: 1.32, 1.79) per 1,000 person-years (PY). The highest mortality rates were observed for lung (0.56 per 1,000 PY; 95%CI 0.44, 0.73) and liver cancer (0.18 per 1,000 PY, 95%CI 0.12, 0.28). The risk of death due to NADM was 76% higher than that of the general population (SMR = 1.76, 95%CI 1.51, 2.06). SMRs decreased with increasing age (fig.). The highest SMRs were observed for Hodgkin lymphoma (20.04, 95%CI 9.55, 42.03) and anal cancer (12.99, 95%CI 3.25, 51.94). Independent risk factors for NADM mortality included: acquired infection through heterosexual (HR = 1.48; 95%CI 1.07, 2.03) *vs.* homo/bisexual contact, time-varying active smoking (HR = 2.23; 95%CI 0.96, 5.18), time-varying presence of hepatitis C virus infection (HR = 1.74; 95%CI 1.09, 2.78) or hepatitis B surface antigen (HR = 2.02; 95%CI 1.12, 3.66) and decreasing time-varying CD4 count (8.49; 5.46, 13.20 for CD4 < 200 cells/µl, 4.10; 2.57, 6.55 for CD4 200-349 cells/µl; 2.50; 1.64, 3.80 for CD4 350-499 cells/µl compared to CD4 ≥ 500 cells/µl).

Figure 1. Mortality rates and SMRs according to age



	<25	30	35	40	45	50	55	60	65	70	>=75
Rate	0.15	0.3	0.57	0.54	2.3	2.36	4.28	7.02	7.88	8.11	13.99
SMR	2.94	3.66	4	1.83	3.35	1.61	1.59	1.61	1.24	0.89	0.96

Conclusions: In PLWH, deaths due to a NADM account for a 20% of overall deaths, of which lung cancer is the most frequent cause. PLWH have a higher risk of NADM-related death compared to the

general population, mainly at younger ages. Life-style factors, such as smoking and infection for hepatitis, as well as immunosuppression are associated with increased risk of NADM mortality.

CO-08. LIFE EXPECTANCY OF PEOPLE WITH HIV ON ANTIRETROVIRAL THERAPY IN SPAIN

I. Jarrín[1], J. del Romero Raposo[2], M. Rava[1], R. Polo[3], A. Koerting[3], J. Portilla[4], J. Peraire[5], V. Estrada[6], S. Ibarra Ugarte[7], G. Samperiz[8] and J. del Amo[3]

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Objectives: We aimed to estimate life expectancy (LE) (or, equivalently age at death) of people with HIV (PWH) who started antiretroviral therapy (ART) in Spain in 2004-2019, and describe causes of death.
Methods: We analyzed antiretroviral-*naïve* individuals from the Cohort of the Spanish AIDS Research Network (CoRIS) who started ART aged ≥ 20 years between January 1, 2004 and November 30, 2019. We calculated LE at age 40 for men and women who started ART in 2004-2013 and 2014-2019, and also stratified by transmission category (men who have sex with men [MSM], heterosexuals [HTX], injecting drug users [IDU]), CD4 count (< 200, 200-349, ≥ 350 cells/µL) and AIDS diagnosis at ART initiation. LE in 10-year age bands within each key population group were estimated using life tables constructed from mortality rates estimated through multivariable Poisson regression models. LE estimates in PWH were compared with those of the Spanish general population, obtained from the National Institute of Statistics.
Results: Of 14,194 individuals, 85% were men and 60% MSM. Median age at starting ART was 37 (IQR:30-44) years, 41% initiated with CD4 ≥ 350 cells/µL and 13% had a previous AIDS diagnosis. During 73,734 person-years (py) of follow-up, 593 persons died [mortality rate: 8.0 (95%CI: 7.4-8.7) per 1,000 py]. LE increased from 68.7 (95%CI: 68.2-69.1) in 2004-2013 to 73.0 (71.9-74.1) in 2014-2019 in men (general population comparators 79.8 and 81.2 years, respectively) and from 68.2 (66.9-69.4) to 72.3 (70.1-74.5) in women (general population comparators 85.4 and 86.4 years, respectively). Non-AIDS related deaths accounted for 68% and 78% of deaths among men and women, respectively: the most frequent causes were non-AIDS defining cancers, mainly lung cancer, liver diseases and non-AIDS infections. For both men and women, LE was longer when starting ART with higher CD4 counts and without AIDS. For men starting ART in 2014-2019 without AIDS and with CD4 < 200, LE was 75.0 (95%CI: 74.3-75.8), rising to 78.3 (77.6-78.9) with CD4 ≥ 350 cells/µL. Corresponding figures for HTX and IDU were 70.1 (69.3-70.9) and 76.1 (75.5-76.8), and 61.2 (60.5-62.0) and 69.2 (68.4-69.9), respectively. For women starting ART from 2014 without AIDS, LE increased from 71.1 (70.9-72.4) to 77.5 (76.9-78.2) among HTX and from 63.5 (62.7-64.3) to 70.9 (70.1-71.6) among IDU.
Conclusions: LE of PWH starting ART in recent years with high CD4 counts and without an AIDS diagnosis approaches that of the general population, especially among MSM, indicating the importance of early diagnosis and sustained treatment.

Sesión de Comunicaciones Orales 2
29 de noviembre – 10:15-12:15h

CO-09. *MONKEYPOX* OUTBREAK IN HIV PATIENTS IN SPAIN, APRIL– SEPTEMBER 2022

M. Ruiz-Algueró, L. Simón, V. Hernando, M.T. Villegas, M. Sastre and A. Díaz

Instituto de Salud Carlos III, Madrid.

Introduction: Globally, *monkeypox* outbreaks are spreading like never before. Since the start of the *monkeypox* outbreak and as of 1 September 2022, the European Centre for Disease Control and Prevention (ECDC) has reported over 18 463 confirmed cases of *monkeypox* (MPX) from 29 EU/EEA countries. Spain has the highest tally in Europe and second only after the United States globally.
Objectives: To describe the national cases of *Monkeypox* among HIV patients.
Methods: Descriptive study of *Monkeypox* cases in HIV patients notified to the National Surveillance Network (RENAVE) network.
Results: From 26/04/2022 to 06/09/2022, 6,749 new *Monkeypox* diagnoses were reported to RENAVE in Spain from 17 Autonomous Regions, and 35.3% (n = 2.382) had HIV infection. Overall, 99.8% (n = 2.376) of HIV-infected people were male, the median age was 39 years (Interquartile Range (IQR): 33-46). The highest percentage were between 30-39 years (38.7%). 39.6% (948 cases) were born in Spain, followed by 33.5% (197 cases) from Latin America. *Monkeypox* transmission was suspected to have occurred through sexual activity in 84.3% of the persons with HIV infection. The majority of those with information, 99.3% (2.064) were men who have sex with men, 0.6% (n = 12) were heterosexual men and 0.1% (n = 3) were heterosexual women. Ninety seven (4.0%) HIV patients have received smallpox vaccine in their childhood, out of them 59.8% (n = 58) were over 40 years of age. A 52.6% (n = 51) of those vaccinated were from Latin America. No significant differences have been observed for the aforementioned characteristics in comparison to non-HIV population. In the HIV subgroup, 79.5% (n = 1.893) presented general symptoms, 39.2% localized rash around the genitals or anus and 41.5% in the mouth. Common systemic features included fever (42.1%), myalgia (41.2%), sore throat (41.6%) and headache (38.8%); lymphadenopathy was also common (37.2%). The percentage cases with complications was 8.5% (n = 160); the main complications were mouth ulcers (n = 55), soft-tissue superinfection (n = 21), genital ulcers (n = 2), rectal ulcers (n = 2) and eye lesions (n = 1). 97 (4.4%) cases were hospitalized, no deaths were reported and none required intensive care unit admission. The clinical presentation and complications were similar among persons with HIV infection and those without HIV infection except for proctitis that was present in six patients and two patients respectively.
Conclusions: More than one third of the *Monkeypox* reported cases in Spain were HIV infected people. We have not found significant differences regarding clinical presentation and evolution between HIV and non-HIV subjects.

CO-10. UNA DE CADA DOS PVIH QUE DESARROLLA DM2 EN 5 AÑOS TIENE RESISTENCIA A LA INSULINA AL DIAGNÓSTICO DE LA INFECCIÓN POR VIH (*RIS-EPICLIN 20_2019*)

M.L. Montes Ramírez[1], C. Busca[1], M. Lagarde[2], J.A. Iribarren[3], J.I. Bernardino[1], J. Olalla[4], L. Martín-Carbonero[1], I. Suárez-García[5], V. Moreno[1], M. Górgolas[6], E. Valencia[1], R. Micán[7], J.R. Arribas[1], R. Montejano[1] y J. González[1].

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CO-10. Tabla

	No desarrollan diabetes				Sí desarrollan diabetes				p
Basal	N	Mediana	P 25	P 75	N	Mediana	P 25	P 75	
ALT	4.956	24	17	36	102	25,5	18	37	0,38
AST	4.824	24	20	31	98	24	20	35	0,59
Colesterol total	4.850	159	138	183	93	154	126	184	0,49
Colesterol HDL	4.375	39	32	47	77	35,5	29	44	0,009
Triglicéridos	4.925	97	71	136	98	121	95	172	0,001
Glucosa	2.465	90	83	96	71	100	88	111	0,001
IMC	2.219	23	21,5	25,8	37	27,1	23,7	30,8	0,001
APRI	4.702	0,29	0,22	0,42	95	0,3	0,23	0,48	0,32
FIB4	4.686	0,83	0,61	1,19	95	1,16	0,73	1,59	0,001
TyG	2.260	8,35	8,04	8,74	64	8,72	8,47	9,03	0,001
TyG RI	2.260	4,52	4,37	4,71	64	4,7	4,58	4,86	0,001

TyG: Índice triglicéridos/glucosa > 8,38 indica esteatosis hepática. TyG: Índice triglicéridos/glucosa Resistencia a la insulina > 4,68.

Marbella. [5]Hospital Universitario Infanta Sofía, Madrid. [6]Hospital Universitario Fundación Jiménez Díaz, Madrid. [7]Hospital Universitario La Paz, Madrid.

Introducción: La diabetes mellitus tipo 2 (DM2) es una de las enfermedades más incidentes en población general. El estudio RIS-EPI-CLIN20_2019 mostró una incidencia elevada de DM2, 15 casos por 1.000 personas-año, en las PVIH mayores de 50 años en la cohorte CoRIS. Nuestro objetivo es describir qué características metabólicas tienen en el momento del diagnóstico de la infección por VIH las personas que desarrollarán DM2 durante el seguimiento.
Métodos: Se analizaron 6.007 pacientes incluidos en CoRIS que iniciaron TAR entre enero de 2010 y noviembre de 2019, sin coinfección por VHB ni VHC. Se registraron 119 diagnósticos de DM2 durante 5 años de seguimiento.
Resultados: En la visita basal la edad mediana (IQR) fue 35 años (29–43), el 12% mujeres, 9,5% estadio C3, mediana de linfocitos CD4+ 375 cel/µL (224-534). La edad, los valores de glucosa, triglicéridos, e IMC fueron significativamente superiores en el momento basal, previo al inicio del TAR, en aquellos que desarrollaron DM2 en los siguientes 5 años. Así mismo, se calcularon marcadores no invasivos de resistencia a la insulina, esteatosis y fibrosis hepática y también se observaron diferencias significativas basales en los que desarrollaron DM2 (tabla).
Conclusiones: Las PVIH que desarrollan DM2 en su proceso de envejecimiento presentan una prevalencia muy elevada de resistencia a la insulina previo al inicio del TAR. Los pacientes con reciente diagnóstico de infección por VIH en los que se determinen alteraciones metabólicas relacionadas con la resistencia a la insulina se deben monitorizar estrechamente e implementar las medidas adecuadas para reducir su impacto.

CO-11. UNDERSTANDING METABOLIC FATTY LIVER DISEASE IN VERTICALLY-HIV INFECTED CHILDREN AND YOUTHS: THE ROLE OF THE INFLAMMASOME

I. Carrasco García[1], L. Escosa[2], Á. González-Domínguez[3], T. Belmonte[3], J. Riscart[3], J. Hurtado[2], M.L. Montes[2], A. Olveira[2], J.I. Bernardino[2], Á. Lancharro[1], C. Busca[2], A. Delgado[2], C. Diez[1], M.L. Navarro[1] and T. Sainz[2]

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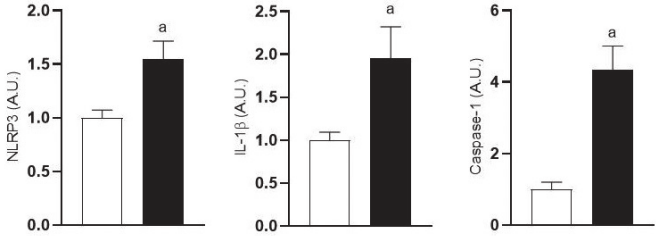
Introduction: The prevalence of metabolic associated fatty liver disease (MAFLD) is high among young people living with perinatally acquired HIV (YLWPH), and only partially explained by overweight and metabolic syndrome defining factors. Recently, activation of the NLPR3 inflammasome has been suggested to be a contributing factor in the development of MAFLD, particularly as a modulator of progression from initial hepatic steatosis to steato-hepatitis. We explored the inflammasome in a cohort of YLWPH, with and without MAFLD.
Methods: Prospective cross-sectional including YLWPH under follow-up in the National cohort (CoRISpe/FARO). MAFLD was diagnosed using non-invasive imaging techniques including a combination of Shear Wave Elastography, Fibroscan and Controlled Attenuation Parameter (CAP). NLRP3 and its final effectors (Caspasa 1 and IL1b) were determined by Western blot and quantified using Image-Lab software (Biorad, Hercules, CA, USA) and compared according to MAFLD status.
Results: We included 23 YLWPH (65% women, 11 diagnosed with MAFLD) with a median of 18 years (12.3-24.4). All were on ART at the moment of inclusion, 91% suppressed. Overweight/obesity was present in 5 (22.7%). NLRP3 was decreased among patients with MAFLD (0,99 [0,88-1,1] *vs.* 1,6 [0,97-2,0], p = 0.02) as it was Il1b (0.97 [0,97-1,13] *vs.* 1,65 [1,1-2,2], p = 0.006) and Caspase-1 (4.33 [4.9-3,7], *vs.* 1.05 [0,92-1,3], p = 0.02). No associations were found between the inflammasome and age, sex, or ethnicity, and no significantly higher values were found among patients with overweight /obesity or those with detectable HIV viral load. NLRP1, but not its final effectors, strongly correlated with the CD4/CD8 ratio (R = 0.69, p = 0.01).

Figure 1. NLRP3 (A) and its final effectors (B-C). White bars represent patients with MAFLD.

Values are means ± SEM. P<0.05 was considered for statistical significance(a)



NLRP3 (A) and its final effectors (B-C). White bars represent patients with MAFLD. Values are means ± SEM. p < 0.05 was considered for statistical significance(a).
Conclusions: Understanding the physiopathology of MAFLD is key in order to design reliable screening strategies and optimize the management of YLWPH in routine clinical practice. Our results do not point out the inflammasome as a potential marker for diagnosis, although the reduced sample size and the absence of biopsy is an important limitation of this study, as steatohepatitis might not be present in this cohort. Further studies addressing the role of the inflammasome as a biomarker of progression to steatohepatitis are needed.

CO-12. LONG-TERM EVALUATION OF RESIDUAL VIREMIA IN A CLINICAL TRIAL OF DOLUTEGRAVIR PLUS LAMIVUDINE AS MAINTENANCE TREATMENT FOR PARTICIPANTS WITH AND WITHOUT PRIOR LAMIVUDINE RESISTANCE

D. Rial Crestelo[1], R. de Miguel Buckley[2], R. Montejano[2], A. Pinto[1], M. Jiménez-González[2], M. Lagarde[1], A. Esteban-Cantos[2], P. Aranguren-Rivas[1], J. Cardiñanos[2], O. Bisbal[1], J.M. Castro[2], M. Santacreu-Guerrero[1], L. Bermejo-Plaza[1], V. Moreno[2], A. Hernando[1], L. Martín-Carbonero[2], R. Rubio[1], R. Delgado[1], J.R. Arribas[2] and F. Pulido[1]

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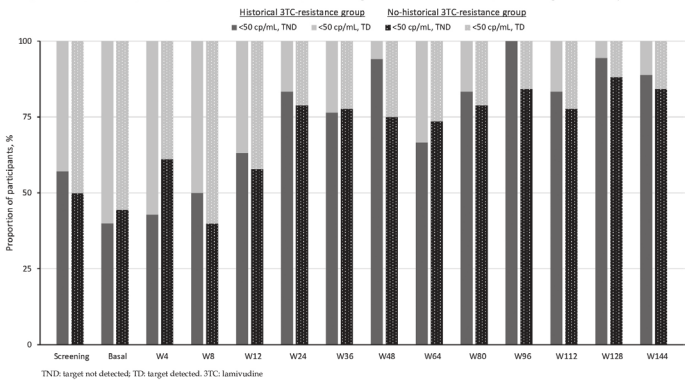
Objectives: To evaluate rates of residual replication using target not detected (TND) after 144 weeks of dolutegravir plus lamivudine in participants with and without past lamivudine resistance.
Methods: Open-label, single-arm, prospective, 144-week pilot clinical trial (NCT03539224.). Virologically suppressed participants were switched to dolutegravir plus lamivudine. We included persons with and without historical RNA lamivudine resistance-associated mutations (RAMs) but without baseline lamivudine RAMs in proviral DNA population sequencing. 144-week efficacy is proportion of participants with < 50 HIV-1 RNA copies/mL, FDA Snapshot intention-to-treat analysis. TND identifies participants with virologic suppression below qualitative detection of HIV-1 RNA.
Results: 41 participants were switched to dolutegravir plus lamivudine, 21 (51.2%) with lamivudine resistance in previous RNA genotype and 27 (65.8%) with lamivudine mutations in baseline proviral DNA retrospectively detected by next generation sequencing. At 144-weeks, 37 participants had < 50 copies/mL HIV-RNA (Table). There were no significant differences in TND between groups. The proportion of participants with TND at week 144 was 88.9% (95%CI: 67.2-96.9) and 84.2% (95%CI: 62.4-94.5) in the group with and without historical lamivudine resistance respectively (Fig.). There were no cases of virological failure.

Figure 1. Proportion of participants with HIV RNA <50 copies/mL target not detected and <50 copies/mL target detected by visit.



Conclusions: In persons without lamivudine RAMs in proviral DNA population sequencing, dolutegravir plus lamivudine remained effective after 144 weeks without any signal of changes in residual viremia based on qualitative detection methods, irrespective of past lamivudine resistance. Larger studies are needed to confirm our findings.

CO-13. TORQUE TENO VIRUS COMO MARCADOR DE RECONSTITUCIÓN INMUNOLÓGICA EN PACIENTES QUE VIVEN CON EL VIH DE TRANSMISIÓN VERTICAL

L. Tarancon-Diez[1], I. Carrasco[1], L. Montes[2], I. Falces[2], S. Jiménez de Ory[1], M. Dapena[3], L. López-Cortés[4], E. Colino[5], A.I. Menasalvas[6], J.A. Iribarren[7], C. Diez[1], I. Bernardino[2], C. Calvo[2], M.Á. Muñoz-Fernández[1], M.L. Navarro[1] y T. Sainz[2]

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Introducción y objetivos: El torque teno virus (TTV), un virus de ADN monocatenario pequeño, circular, es una parte integral del viroma humano, no patogénico. Muchos aspectos de su interacción con el sistema inmune se desconocen, pero estudios recientes han sugerido su potencial como marcador inmunológico en pacientes inmunosuprimidos. El objetivo de este estudio fue medir la carga viral de TTV en una cohorte de pacientes VIH infectados por transmisión perinatal (PVIH) y estudiar su asociación con la reconstitución inmunológica.
Métodos: Se seleccionaron pacientes PVIH en tratamiento antirretroviral (TAR) y con carga viral VIH suprimida de la Cohorte Española de PHIV (CoRISpe/FARO) y se compararon con controles no infectados. Se obtuvieron muestras de plasma y células mononucleares de sangre periférica del Biobanco VIH. Se realizó qPCR para la detección y cuantificación de TTV, que se correlacionó con marcadores de inflamación y activación celular de linfocitos T analizados por citometría multiparamétrica y la evolución inmunovirológica a largo plazo.
Resultados: Se incluyeron un total de 57 PVIH (44% varones) y se compararon con 23 donantes sanos (DS) VIH– (34% varones). Los PHIV eran más jóvenes (20 [17-24] vs. 26 [24-27] años, p < 0,001). Su mediana de CD4 era de 736 [574-906], la mediana de tiempo en TAR de 17 años [14-20,5] y la de supresión viral 65 meses [39-116]. La carga viral de TTV en plasma fue significativamente mayor entre los PVIH (fig. A) y en los hombres en comparación con las mujeres (p = 0,02). Entre los pacientes PVIH, la carga viral de TTV se correlacionó con los niveles de CD4, CD8 y el ratio CD4/CD8 (p < 0,05, fig. B), pero no con el nadir CD4, la edad al inicio del TAR o el tiempo de supresión. Entre los PVIH, la carga viral de TTV se correlacionó positiva-

CO-12. FDA-snapshot at week 144, Intention to treat– exposed analysis population (n = 41)

	All participants (n = 41)	Historical resistance to lamivudine (n = 21)	No historical resistance to lamivudine (n = 20)	p
HIV-1 RNA < 50 copies/mL	37 (90.2)	18 (85.7)	19 (95)	0.61
HIV-1 RNA ≥ 50 copies/mL	0 (0)	0 (0)	0 (0)	
HIV-1 RNA ≥ 50 copies/mL in W144 window	0 (0)	0 (0)	0 (0)	
Discontinuation Study Drug due to Lack of Efficacy	0 (0)	0 (0)	0 (0)	
Discontinuation Study Drug due to other reasons and last available HIV-1 RNA ≥ 50 copies/mL	0 (0)	0 (0)	0 (0)	
No virologic data at W144	4 (9.8)	3 (14.3)	1 (5)	0.61
Discontinuation Study Drug Due to AE	1 (2.4)	1 (4.8)	0 (0)	
Discontinuation Study Drug due to other reasons and last available HIV-1 RNA < 50 copies/mL	3 (7.3)	2 (9.5)	1 (5)	

AE: adverse event.

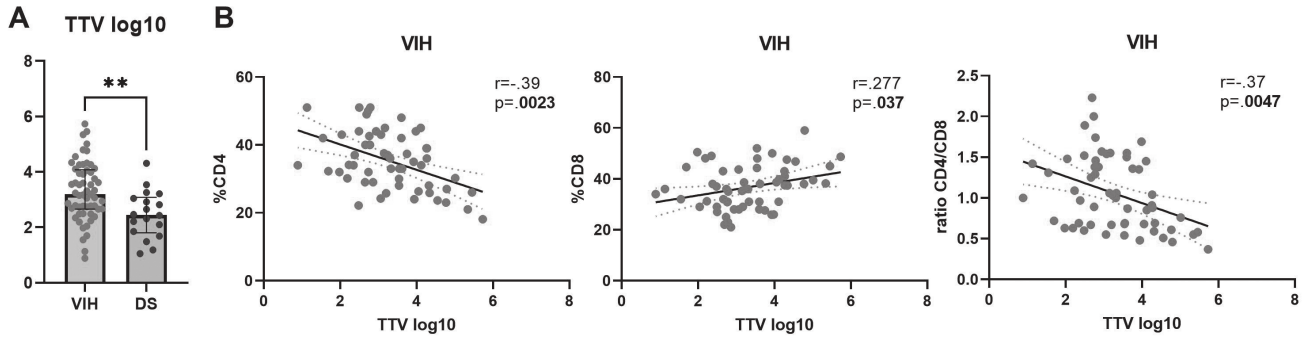

Fig. CO-13

mente con la coexpresión de HLADR/CD38 en células T-CD4 (p < 0,01, r = 0,39) y la IL-6 soluble (p = 0,04, r = 0,37). La carga viral inicial de TTV era mayor en los pacientes que tuvieron fallo virológico durante el seguimiento posterior (p < 0,05) y se correlacionaba inversamente con la evolución del ratio CD4/CD8 a los 3 y 5 años (p = 0,09; r = –0,33 y p = 0,06; r = –0,56).

Conclusiones: La carga viral de TTV fue significativamente mayor entre los PVIH. A pesar de que la correlación con la activación de células T y la IL-6 fueron moderadas, la fuerte correlación inversa con el ratio CD4/CD8 basal y en el seguimiento sugiere que TTV puede tener valor como predictor de la reconstitución inmunológica.

CO-14. IL-18 AND IL-3 IN EXTRACELLULAR VESICLES: BIOMARKERS FOR A DURABLE ELITE CONTROL

E. Poveda[1], W. Fitzgerald[2], C. Reglero[1], M. Crespo[1], A. Mariño[3], H. Álvarez[3], N. Valcarce[3], E. Ruiz-Mateos[4], L. Margolis[2], M.M. Lederman[5], M.L. Freeman[5] and on behalf of ECRIS integrated in the Spanish AIDS Research Network[6]

[1]Instituto de Investigación Sanitaria Galicia Sur, Vigo. [2]National Institute of Child Health and Human Development, Bethesda. [3]Hospital Universitario Arquitecto Marcide, Ferrol. [4]Instituto de Biomedicina de Sevilla, Sevilla. [5]Case Western Reserve University, Cleveland. [6]Spanisch AIDS Research Network, Madrid.

Introduction: Elite controllers (EC) with a durable control of HIV-1 replication may represent a model of functional cure. Extracellular vesicles (EVs) have emerged as a mechanism for intercellular communication by targeted delivery of cytokines. We evaluated the cytokine profile associated with EVs in well-characterized cohorts of people living with HIV (PLWH) with different virological control status, including durable and transient EC.

Methods: 120 donors were included and divided into 5 groups defined as: 30 antiretroviral therapy (ART)-*naïve* (median 7 days after HIV diagnosis); 30 ART-treated with nondetectable viremia (median time on ART 9 years); 30 EC who controlled viremia for a median of 14.4 years [15 transient controllers (TC) who ultimately lost virus control, and 15 persistent controllers (PC) who sustained virus suppression], and 30 HIV-uninfected controls. Levels of 39 pro-inflammatory markers in and on EVs isolated by ExoQUIck from stored plasma were quantified using a multiplexed bead-based Luminex assay. Random forest, principal component analysis, and decision trees were performed to identify specific cytokines as a signature of each study group.

Results: Overall, the median levels of EV-associated cytokines were 1.33-fold higher among PLWH than for the uninfected control group. Among PLWH, EC showed the highest levels of cytokines (1.11– and 1.32-fold higher compared to ART-exposed and ART-*naïve*, respectively). Within the EC group, EV cytokine levels were 1.36-fold higher for PC than TC. Higher levels of IL-18 in EVs best distinguished PLWH from uninfected controls (AUC 0.741). In the context of suppressed viremia (EC and ART-exposed), higher levels of IL-18 were associated with EC (AUC 0.942). IL-18 discriminates between EC and ART-exposed with a sensitivity of 73.3% and a specificity of 100%. 96% of participants with suppressed viremia and IL-18 > 2.23 pg/mL were correctly classified as EC. Finally, within EC, higher levels of IL-3 best distinguished PC from TC (AUC 0.824) with a sensitivity of 73.3% and a specificity of 86.7%.

Conclusions: EC showed higher levels of EV-associated cytokines compared with other PLWH groups. EV-associated cytokine levels were higher for EC with durable control of HIV-1 replication (PC) than for those without (TC). The role of EV cytokines, intercellular communication and endogenous control of HIV expression should be investigated further.

CO-15. BLOCKADE OF TIGIT BUT NOT TIM3 IMPROVES DC-NK CELL BASED IMMUNOTHERAPY AGAINST HIV-1 *IN VITRO* AND IN HUMANIZED MICE

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Introduction: Our previous study showed that expression of TIGIT *versus* TIM3 in Natural Killer cells (NK) from People living with HIV (PLWH) associates with differential abilities to eliminate HIV-1– infected CD4+ T lymphocytes after dendritic cell (DC) stimulation. We asked whether blockade of TIGIT *versus* TIM3 on NK during interaction with DC improves the elimination of HIV-1-infected cells in vitro, and the efficacy of immunotherapy in a humanized mouse model.

Methods: Monocyte-derived dendritic cells from blood samples of n = 9 PLWH on ART with high TIGIT expression, were generated and activated with Poly I:C (PIC) and subsequently incubated for 16h with autologous NK in the presence of anti-TIGIT and/or anti-TIM3. Then, NK were co-cultured for additional 16h with autologous CD4+ T cells in the presence of Romidepsin and Raltegavir. Proportions of p24+ cells in cultured CD4+ and expression of CD56, CD16, CD107a, IFNγ on NK were evaluated by flow cytometry. To address efficacy *in vivo* of anti-TIGIT modulation on NK cells, we intravenously injected NSG mice with NK, PIC-treated DC, and CD4+ from the same PLWH at a 1:2:4 (DC: NK: CD4) ratio. As a control, NSG were also transplanted only with CD4+ T cells from the same PLWH. Anti-TIGIT was administered intraperitoneally every 48h, and n = 10 mice per group were included in two independent experiments. Proportions of p24+ cells in human CD45+ CD4+ T cells in the peripheral blood, liver and spleen at 7 days post injection were analyzed by flow cytometry.

Results: *In vitro*, blockade of TIGIT increased proportions of IFNγ+ CD107a+ NK from PLWH after *in vitro* PIC-DC stimulation, which associated with significant reduction in proportions of autologous p24+ CD4+ T cells (p = 0.0078). Conversely, blockade of TIM3 did not significantly improve activation or function of NK cells. Interestingly, the combination of anti-TIM3 with anti-TIGIT was less effective than anti-TIGIT treatment alone (p = 0.05). Importantly, administration of anti-TIGIT into NSG transplanted with NK cells, DC and CD4+ T cells from PLWH specifically led to a significant reduction of p24+ cells within circulating human CD4+ T cells compared to mice receiving only CD4+ T cells (p = 0.0069). Similar tendencies in frequencies of p24+ CD4+ T cells were present in the liver, while in lymphoid tissue detection of p24+ was lower and similar in all NSG groups.
Conclusions: Collectively, our study suggests that blockade of TIGIT rather than TIM3 is a promising strategy to enhance NK-DC based immunotherapies against HIV.

CO-16. ONE-YEAR TREATMENT WITH PONATINIB INDUCES A SUSTAINED PROTECTIVE EFFECT AGAINST HIV INFECTION IN CD4+ T CELLS FROM INDIVIDUALS WITH CHRONIC MYELOID LEUKEMIA

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Introduction and objectives: *In vivo* treatment with TKIs protects CD4+ T cells from HIV infection and stimulates cytotoxic populations that may eliminate the infected cells. Therefore, PLWH treated with ART and dasatinib show reduced reservoir size that is resistant to reactivation. Our aim was to evaluate the persistence of TKI-mediated protective activity against HIV in CD4 from individuals who received one-year consolidation treatment with ponatinib against chronic myeloid leukemia (CML).
Methods: Nine participants of multicenter, open-label, single-arm, Phase II exploratory trial NCT04043676 were recruited. They achieved deep molecular response against CML after 14 (IQR 5.5-15.5) years of treatment with imatinib before interruption and then received one-year consolidation treatment with ponatinib 15mg/day. Blood samples were taken before starting ponatinib, after 1 year-treatment, and 3, 6 and 12 months after interruption to monitor CML relapse. PBMCs activated with PHA/IL-2 48h were infected with NL4-3_wt 72h. HIV p24 core antigen, SAMHD1 phosphorylation at T592 (pSAMHD1), CD4 memory subpopulations, and cytotoxic cell populations were analyzed by flow cytometry. PBMCs antiviral activity was evaluated by measuring caspase-3 activity in NL4.3_wt-infected TZM-bl cells 48h.
Results: 1) 5 participants (55.5%) did not relapse from CML 12 months after ponatinib interruption (Non-relapsed); 4 participants (44.4%) relapsed after 5,5 months (IQR 4,25-6,75) of ponatinib interruption (Relapsed). 2) CD4 were susceptible to HIV infection in all participants while on treatment with imatinib, but 1 year-treatment with ponatinib reduced 8.8-fold HIV infection in4 these cells (Fig. 1A). This protection was maintained after 12 months of treatment-free remission (TFR) in Non-relapsed (p = 0.0039), which correlated with pSAMHD1 interference. 3) After CML relapse and imatinib reintroduction, all CD4 memory subpopulations regained susceptibility to HIV infection. 4) PBMCs from Non-relapsed showed 2-fold increased antiviral cytotoxicity (p = 0.0317) after 1-year of ponatinib, in comparison with Relapsed (Fig. 1B). Cytotoxic activity was similar in both groups 3-months after interruption and remained increased in Non-relapsed for 11 months. 5) CD8 degranulation activity (CD107a+) increased 4.08-fold (p = 0.0317) 3-months after interruption in Non-relapsed. Levels of CD3+CD8-TCRγδ + cells increased in both groups (p = 0.0330) since treatment withdrawal but their degranulation capacity was only significantly increased 3.3-fold (p = 0.0078) after ponatinib withdrawal in Non-relapsed.

Figure 1A

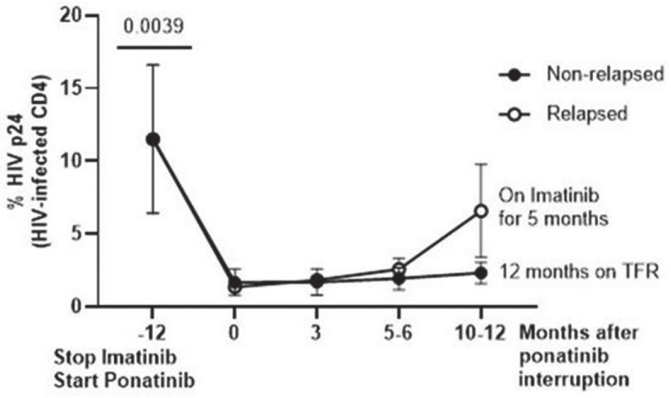
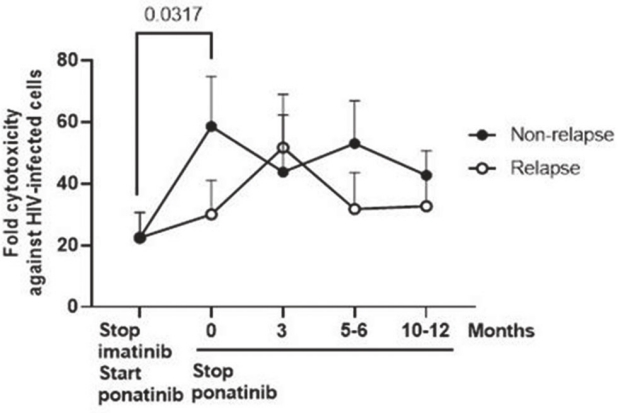


Figure 1B



Conclusions: One-year treatment with ponatinib preserved SAMHD1 antiviral activity in CD4+ T cells and induced a potent sustained cytostatic and cytotoxic effect, impeding HIV infection. The antiviral protection was maintained at least 12 months during TFR in correlation with sustained antileukemic response. Intensification treatment with TKIs could be useful for HIV cure strategies.