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Comunicaciones orales

XI Congreso Nacional GeSIDA y XIII Reunión Docente de la Red de Investigación de Sida (RIS)

Toledo, 10-13 de diciembre de 2019

Sesión de Comunicaciones Orales 1 - Miércoles, 11 de diciembre, 10:15-12:15 h

OR-01. HIV/HBV COINFECTION IN SPAIN: PREVALENCE AND CLINICAL CHARACTERISTICS

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Objectives: We assessed the prevalence of HIV/HBV coinfection in Spain in 2018 and compared the results with similar 5 similar studies performed since 2002.
Methods: The study was nested in a survey designed to assess the prevalence of HCV infection in 43 centers during October-November 2018. Patients were selected using simple random sampling. We evaluated the presence of HBsAg, HBV-DNA, HDV antibodies (Ab), anti-HBV therapy, and liver fibrosis. Cirrhosis was defined by liver biopsy, transient elastography (> 12.5 kPa), and clinical/biological findings.
Results: The reference population was 40,650 patients living with HIV (PLWH), and the sample size was 1,733. HBsAg serostatus was known in 1,673 patients (96.5%) and 54 (3.2%) were HBsAg-positive, 7 (13.0%) of whom had cirrhosis. No significant differences were found in the prevalence of HCV-Ab between HBsAg positives and negatives (40.7% vs. 32.7%, p = 0.445), but spontaneous HCV clearance was more frequent among HBsAg positives in comparison with HBsAg negatives (54.5% vs. 17.0%, p < 0.001). Of the HIV/HBV-coinfected patients, 38 (70.4%) had known serostatus for HVD, 10 of whom (26.3%) had HDV-Ab. All HIV/HBV coinfected patients were receiving anti-HBV therapy, and 33 (61.1%) had HBV DNA determined in the previous 12 months, 32 of whom (97.0%) had HBV DNA < 80 IU ml. Main findings in the five national cross-sectional studies are shown in the table.

Trends in HIV/HBV coinfection in Spain

	2002	2009	2015	2016	2017	2018
Centers - n	39	43	41	43	43	43
Reference population - n	31,800	29,559	35,791	38,904	40,322	40,650
Sample size - n	1,260	1,458	1,867	1,588	1,690	1,733
Tested for HBsAg -%	92.7	97.7	97.1	97.5	96.2	96.5
HBsAg (+) among those tested - %	4.9	3.4	3.0	3.9	3.0	3.2

Conclusions: The prevalence of HIV/HBV coinfection in Spain in 2018 was 3.2%, a figure that remained stable since 2002. Most HIV/HBV-coinfected patients had complete suppression of HBV DNA, but HDV-coinfection and cirrhosis are common problems in this population group. Chronic HBV infection is soon to be the most prevalent chronic viral hepatitis among PLWH in Spain.

OR-02. PROFILAXIS PREEXPOSICIÓN AL VIH EN ESPAÑA: RESULTADOS FINALES DEL ESTUDIO DE FACTIBILIDAD DE IMPLEMENTACIÓN DE LA PREP

C. Iniesta[1], R. Polo[2] y Grupo de Trabajo de la PrEP en España[3]

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Introducción: España debe adaptar la implementación de PrEP a las características de sus Sistema Sanitarios. El estudio de implementación de la PrEP puesto en marcha por el Ministerio de Sanidad ha evaluado 3 circuitos: Centro de ITS hospitalario, Centro de ITS extrahospitalario y Centro comunitario. El objetivo es evaluar la factibilidad de la implementación de la PrEP en España. En este trabajo se analizan los resultados clínicos y conductuales finales del estudio.
Métodos: Estudio observacional post-autorización realizado en 4 centros (BCN Checkpoint, Unidad de ITS Drassanes, Centro de ITS de Donostia y Hospital General de Valencia). Se incluyeron hombres que tienen sexo con hombres (HSH) y mujeres trans, entre 18-65 años, con criterios de PrEP. Se recogió información epidemiológica, clínica, conductual y de factibilidad. Periodo de estudio 11/2017-07/2019, en

que el 95% de participantes había completado el seguimiento. Se analiza adherencia a la PrEP (SMAQ), uso de preservativo, diagnóstico de ITS y uso de drogas. Las diferencias con información basal se contrastaron mediante el test de simetría de Bowker. Los datos de factibilidad están siendo analizados en el momento de este envío.
Resultados: Se incluyeron 327 personas. La edad mediana fue 36 años, el 99,1% fue HSH, 22,0% de origen latinoamericano, 67,3% universitarios y 86,5% trabajaba. No hubo seroconversiones. El 19,3% abandonaron, y sólo 2 lo hicieron por efectos secundarios leves. 248 participantes completaron 52 semanas de seguimiento. Comparando la semana basal y la 52, el uso de preservativo habitual pasó del 58,0% al 30,0%, ($p < 0,001$). Hay una tendencia al aumento la frecuencia de gonorrea -21 (8,5%) a 29 (12,0%)-, sífilis- 6 (2,4%) a 11 (4,4%)- y clamidia -18 (7,3%) a 22 (8,9%)- aunque ninguna estadísticamente significativa. La adherencia a PrEP pasó del 79 al 86% medida con SMAQ y la frecuencia de personas que no había olvidado ninguna toma en la última semana se mantuvo en 94%. El uso de drogas pasó del 75,0% al 62,0%($p < 0,001$). Las más consumidas basalmente fueron Popper, GHB, cocaína y MDMA y en la semana 52 alcohol, popper, GHB y cocaína. Hubo un descenso significativo del uso de cocaína, GHB, popper, speed, mefedrona, MDMA, y mentanfetamina.
Conclusiones: La PrEP es eficaz, segura y su implementación. No se produjeron infecciones por VIH y la frecuencia de ITS no aumentó significativamente. Se mantuvo una adherencia elevada y el uso de la mayoría de las drogas descendió, así como el uso de preservativo. A partir de estos datos la implementación de la PrEP se muestra factible.

OR-03. ALTA ACEPTABILIDAD Y EFECTIVIDAD DE UNA INTERVENCIÓN ONLINE DE AUTO TOMA PARA VIH EN HOMBRES QUE TIENEN SEXO CON HOMBRES EN ESPAÑA. RESULTADOS PRELIMINARES

C. Agustí Benito[1], R. Muñoz[1], V. González[1], J. Hoyos[2], E. Muntada[1], S. Moreno[1], P. Romano[1] y J. Casabona[1]

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Objetivos: El objetivo del estudio fue evaluar la aceptabilidad y efectividad de una intervención online de auto toma de muestra para la realización de la prueba del VIH y posterior consulta de resultados online dirigida a hombres que tienen sexo con hombres (HSH) usuarios de páginas y aplicaciones móviles de contactos gays en España.
Métodos: Se diseñó la web www.testate.org para ofertar la prueba, consultar los resultados y recoger información sociodemográfica y conductual. Ésta se publicitó en: Grindr, Wapo, PlanetRomeo, Bakala, MachoBB y Trans4men. Tras firmar el consentimiento informado online, los participantes solicitaron el envío a su domicilio de un kit para auto toma de saliva por correo y un sobre con franqueo pagado para enviar la muestra al laboratorio de referencia. Los participantes recibieron un recordatorio por SMS o email para repetir la prueba a los 3, 6 o 12 meses. Un mes después de que consultaran el resultado, se llamó por teléfono a los participantes reactivos. Se realizó una encuesta de aceptabilidad anónima a todos los participantes.
Resultados: De noviembre 2018 a junio 2019 se recibieron 2.031 solicitudes y 1.236 muestras (60,9% tasa de retorno) que correspondieron a 1.125 participantes procedentes de todas las provincias de España. 1.022 participantes (90,8%) se realizaron una sola prueba, 96 (8,6%) y 7 (0,6%) participantes se realizaron 2 y 3 pruebas respectivamente. La mediana de edad fue de 32 años. El 22,4% eran extranjeros. El 24,5% residían en ciudades con menos de 50.000 habitantes. El 25,5% no se habían realizado la prueba anteriormente. El 44,9% no habían utilizado preservativo en su última relación anal. El 32,8% habían tenido una ITS en los últimos 5 años. Se detectaron 32 resultados reactivos (2,6%), 2 de ellos en participantes repetidores. De los 17 participantes con criterios de búsqueda activa, se logró contactar a 13 (73,4%). De éstos, 12 habían confirmado el resultado y estaban en seguimiento y 1 fue un falso positivo. El 95,1% de los participantes declararon que repetirían la experiencia y el 97,6% la recomendarían a un amigo. Las ventajas más identificadas fueron la comodidad y privacidad.
Conclusiones: La intervención fue bien aceptada por la población a la que iba dirigida. Se accedió a una población a riesgo elevado frente el VIH. Se observó una elevada efectividad en identificar una elevada proporción de participantes infectados que lo desconocían así como de participantes vinculados al sistema sanitario.

OR-04. SURVEILLANCE OF CLINICALLY RELEVANT RESISTANCE TO FIRST LINE ARV REGIMENS IN SPAIN: 2018 UPDATE

C. Guerrero Beltrán[1], A. de Salazar[1], M. Álvarez[1], J. Olalla[2], M. García Álvarez[3], J.A. Iribarren[4], M. Masiá[5], M. Montero[6], S. García Bujalance[7], M. Rivero[8], L.J. García-Fraile[9], C. Rodríguez[10], A. Iborra[11], A. Imaz[12], D. García Rosado[13], J. Peraire[14], J. Portilla[15], E. Caballero[16], M.J. Pérez Elías[17] and F. García[1]

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Introduction and objectives: Initial regimens currently recommended by treatment guidelines include high genetic barrier antiretrovirals (ARVs), thus it may be of interest to evaluate the clinically relevant resistance. Here, we present data on clinically relevant transmitted drug resistance to ARVs recommended for first-line treatment in Spain during the period 2007-2018, including the last update.
Methods: We analysed 6090 RT & Pro Fasta sequences from CoRIS (2007-2018). As Integrase resistance is not part of routine testing in naïve patients in Spain, we run a surveillance programme (2012-2018) and tested 1404 patients. We evaluated the prevalence of clinically relevant TDR by using Stanford v8.7 Algorithm. First line regimens for each study period were those recommended by the Spanish treatment guidelines (GESIDA).
Results: Clinically Relevant resistance to recommended 1st line regimens showed a slow decline from 2007-2012 and peaked in 2013-2014 due to the inclusion of Rilpivirine for 1st line in the Spanish recommendations. Detailed results for 2007-2018 are shown in the table below:

Period	NRTIs (%)	NNRTIs (%)	PIs (%)	INsTIs (%)
2007 (n = 482)	3.3	5.6	1.4	*
2008-2009 (n = 1,169)	3.5	4.3	0.6	*
2010-2011 (n = 1,298)	1.6	4.5	0.6	*
2012 (n = 555)	2.5	4.7	1.1	0.2 (n = 194)
2013 (n = 577)	1.2	8.1	0.9	
2014 (n = 582)	1.7	10.1	1.4	0 (n = 98)
2015-2017 (n = 821)	2.1	*	*	0.2 (n = 817)
2018 (n = 606)	0.8	*	*	1.0 (n = 295)

*ARVs not recommended for 1st line.

Conclusions: Our results indicated that clinically relevant TDR to approved first line regimens showed a slow decline from 2007 to 2018. Resistance to INSTIs remains at very low levels. These findings, together with the very low prevalence of resistance to recommended first line NRTIs in 2015-2018 reinforce GESIDA recommendations on baseline resistance testing and test and treat strategies when starting PI or INSTI based regimens.

OR-05. TARGETING NUCLEIC ACID SENSORS IN DENDRITIC CELLS DIFFERENTIALLY RESTORES FREQUENCIES VERSUS POLYFUNCTIONALITY OF HIV-1 SPECIFIC CD8+ T CELLS ON TREATED CHRONIC HIV-1 INFECTED PATIENTS

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Introduction: Anti-retroviral therapy (ART) efficiently inhibits HIV-1 replication, but it cannot eliminate HIV-1 latently-infected reservoir cells. Inability of exhausted cytotoxic CD8+ T lymphocytes (CTL) to kill such persistent cells in patients on ART highlights the necessity of reinvigorating HIV-1-specific immune responses. Activation of nucleic acid sensors in dendritic cells (DC) is associated with induction of effective polyfunctional HIV-1-specific CTL (pCTL) in controllers. Our objective is to evaluate whether stimulation of nucleic acid sensors on DCs from treated chronic HIV-1 infected patients will enhance activation of HIV-1 specific pCTL responses.
Methods: DC were generated *in vitro* from CD14+ monocytes isolated from the blood of chronic HIV-1+ patients in the presence of GMCSF and IL4 (MDDC). MDDCs were cultured in media or with a pool of HIV-1 Gag peptides alone or in combination with STING and TLR3 agonists for 24h. Subsequently, DCs were incubated with autologous CD8+ T cells and induction of IFNγ+ CD107a+ pCTL was evaluated by FACS. Samples from n = 21 chronic HIV-1 patients on ART with undetectable plasma viremia were included in the study. In some experiments, patients were stratified by time of ART initiation. Finally, CD4+ T cells from chronic HIV-1+ patients were cultured with 30 μM Raltegavir and 50 nM Romidepsin in the absence or the presence of autologous CD8+ T cells pre-incubated with unstimulated or activated MDDCs and gag peptides. Proportions of intracellular p24+ CD4+ T cells were assessed by FACS after 24h.
Results: Two distinct groups of HIV-1+ patients were identified, with either high or low basal CD8+ T cell responses to autologous MDDC loaded with Gag peptides. Simultaneous activation of MDDC with STING and TLR3 agonists improved the proportions of Gag-specific pCTL in high responders. On the other hand, treatment with adjuvant-stimulated MDDC significantly restored frequencies of total Gag-specific CD8+T in low responders. Interestingly, we also observed that high responder patients were significantly enriched in individuals on ART treatment for more than 10 years. Therefore, defined chronic patients might differentially benefit from adjuvant-conditioned MDDC therapy. Importantly, CD8+ T cells from chronic patients stimulated with adjuvant-treated MDDC and gag peptides reduced frequencies of p24+ within CD4+ T cells in contrast to those cells incubated with control unstimulated MDDC.
Conclusions: Personalized adjuvant targeting of STING and TLR3 in DC is a promising strategy to boost HIV-1 specific pCTL responses in treated chronic HIV-1 patients and might be useful for the design of future therapeutic strategies to eliminate HIV-1 infection.

OR-06. EXPLORING THE THERAPEUTIC POTENTIAL OF FABS DERIVED FROM NOVEL ANTI-SIGLEC-1 MABS WITH THE ABILITY TO BLOCK HIV-1 CAPTURE

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Dendritic cells (DCs) can capture HIV-1 particles and transfer them to nearby $CD4^+$ T cells through a mechanism called *trans*-infection. This process depends on Siglec-1, a receptor expressed on the surface of DCs and up-regulated upon cell maturation. Siglec-1 recognizes sialyllactose-containing gangliosides in the viral envelope of HIV-1. We have recently generated and characterized new anti-Siglec-1 monoclonal antibodies (mAbs), which efficiently block this interaction. Antigen-binding fragments (Fabs) lack the antibody crystallisable fragment (Fc) of a mAb, and therefore have a lower risk to trigger Fc-mediated autoimmunity against the Ab treatment. Because of their reduced size, Fabs have an effective tissue penetrating capacity, which could be key to reach lymphoid tissues. Although the serum half-life of Fabs is extremely short, recent studies show that PEGylated Fabs have increased half-life and stability in clinical applications. Here we aimed to investigate if Fabs derived from these novel anti-Siglec-1 mAbs are able to efficiently block viral capture mediated by Siglec-1 to assess their therapeutic potential and inhibit HIV-1 *trans*-infection. Four anti-Siglec-1 blocking mAbs (named 1F5, 5B10, 3F1 and 4E8) were used to produce Fabs. Proper mAb cut was assessed by SDS-PAGE analysis and FACS staining using an anti-Fc mAb. The blocking capacity and the IC_{50} were measured using Raji cells stably transfected with Siglec-1. Raji Siglec-1 cells were pre-incubated with serial dilutions of purified Fabs and at a constant concentration of fluorescently labelled HIV viral like particles (VLPs). The viral capture capacity was measured by FACS. Fab HIV blocking capacity was confirmed on DCs. Statistical differences were assessed with a Wilcoxon non-parametrical test. Fabs from 1F5 and 5B10 mAbs were efficiently produced, as confirmed both by SDS-PAGE and Fc labelling assays. Preliminary results indicate that both Fabs and mAbs display a similar IC_{50}. In addition, both original mAbs and Fabs were able to block > 98% of HIV VLP capture in Raji Siglec-1 cells ($p \leq 0.0001$) and mature DCs. Moreover, fluorescent wild type HIV-1 uptake was also efficiently blocked in mature DCs. Since anti Siglec-1 Fabs block HIV-1 capture on primary DCs, these potential antivirals could be used in combination with Anti-Retroviral Therapy (ART) to reach lymphoid tissues and block HIV-1 *trans*-infection.

OR-07. IMMUNOLOGICAL AND CYTOKINE CHANGES IN BLOOD AND GUT MUCOSA FROM PHI BY AN EARLY ART

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Introduction: The initiation of ART during primary HIV-1 infection (PHI) decreases transmission, contains viral reservoir establishment, prevents damage to immune system and reduces immune activation. The aim of this study was to analyse immunological changes in cell subsets in blood and rectal tissue as well as mucosal cytokine profile after initiating an intensified-5-drug ART regimen during very early PHI.

Methods: Patients started an intensified ART consisting on abacavir/lamivudine/dolutegravir regimen during 48 weeks plus darunavir-r and maraviroc the first 12 weeks. Rectoscopies were done at w0 and w48. Immunological subsets in blood (PBMC) and rectal tissue (MMC) were compared between w0 and w48 and between cases (Fiebig I-II, n = 6) and controls (Fiebig II-IV, n = 11) by multi-parametric flow cytometry. The analysis of 25-cytokines on rectal fluid was performed using Luminex assay. Clinical Trials NCT02588820.

Results: At w48, all except one patient in the controls have undetectable plasma VL. At w48, a higher increase of blood $CD4^+$ T cells was observed in cases (from 39.05% to 47.47% p = 0.031) than in controls (from 36.50% to 36.10%, p > 0.05). CD4/CD8 ratio was also higher in cases both in PBMCs and in MMCs. ART highly decreased activated $CD8^+$ T cells in both cases (from 24.3% to 12.6%, p = 0.0313) and controls (from 30.1% to 7.5%, p = 0.004) from PBMCs and MMCs (from 39.55% to 22.80% in cases, p = 0.0087 and from 52.8% to 36.9% in controls, p = 0.004). Concerning naïve $CD4^+$ and $CD8^+$ T cells, higher percentages were seen in cases with respect to controls even before initiation of ART and were maintained at week 48. Moreover, CD8+ T_{SCM} cells were higher in cases before and after ART (p = 0.014 and p = 0.005, respectively). At mucosal tissue, percentage of macrophages ($CD11c^+$ $CD163^+$) was higher in controls than in cases (p = 0.009) at w0 and decreased in controls (p = 0.006) at w48. In general, a decrease of pro-inflammatory cytokines, such as IL-8, occurred mainly in samples from cases at w48 (p = 0.008). In addition, levels of Th1 (IFN-γ, IL-12, MIP-1β), Th2 (IL-4, IL-10) and Th17 cytokines and chemokines decreased similarly in both cases and controls at w48.

Conclusions: An extremely early intensified ART in PHI patients allowed good immunological recovery in different body compartments being associated with better immunological reconstitution, decreased immune activation and decreased pro-inflammatory profile in mucosa.

OR-08. SHORT-TERM INCREASE IN RISK OF OVERWEIGHT AND CONCOMITANT SYSTOLIC BLOOD PRESSURE ELEVATION IN TREATMENT NAÏVE PERSONS STARTING INSTI-BASED ANTIRETROVIRAL THERAPY

J.A. García, R. Galdámez Fuentes, M. Fernández-González, C. Robledano, V. Agulló, J. García-Abellán, G. Telenti, S. Padilla, F. Gutiérrez and M. Masiá

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Introduction: Integrase strand transfer inhibitors (INSTI) have been associated with weight gain, but their effect on short-term overweight/obesity incidence, blood pressure (BP) and metabolic markers change has not been described in treatment-naïve persons living with HIV (PLWH).

Methods: Medical records of treatment-naïve persons starting ART at the HIV Clinic of University Hospital of Elche (Spain), between January 2007 and July 2019 were retrospectively reviewed. Standard procedures included measurements of weight, BP and metabolic assessment. Data at baseline, 48, 72, and 96 weeks post ART initiation were analysed. We used Cox mixed-effects model to generate predictions of BMI over time and Generalized Additive Mixed Models (GAMM) to relax the linearity assumptions and generate 95% confidence intervals in the multivariable adjust.

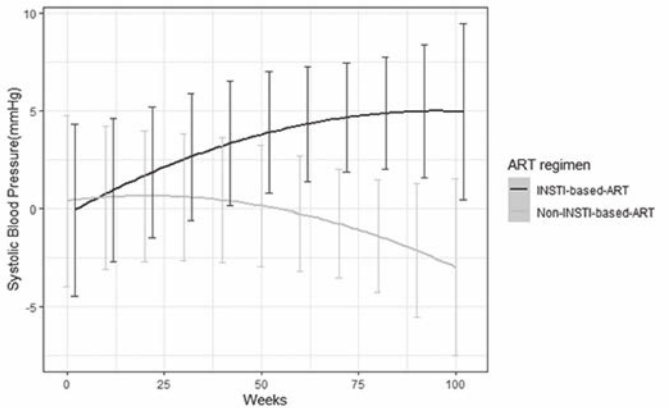
Results: Among 219 (median age 44.0 years, IQR = 37.0-53.5; 46 females) participants. Baseline weight mean (SD) was 70.4 (13.7) kg without difference between regimens; 66% had a BMI < 25 kg/m^2. The incidence of overweight/obesity was significantly greater in persons starting INSTI-based regimens (Table 1): 15 (36.6%) of 41 patients treated with INSTI vs. 30 (28.9%) of 104 treated with other ART regimens (HR 1.8, 95%CI, 1.1-3.3; p = 0.046). In contrast to other ART regimens, patients treated with INSTI showed a significant increase in systolic BP(SBP) (adjusted increase 6.6 mmHg, 95%CI, 0.4-13.1; p = 0.048) (Table 2 and Figure) that was correlated with weight gain (r = 0.13, 95%CI, 0.10-0.16; p < 0.001). Patients who reached overweight/obesity in INSTI-based ART showed a significant increase in LDL cholesterol.

Table 1. Factors Associated with the Development of Overweight/Obesity post ART initiation

Factor	Adjusted HR (95% CI)	*p*-value
INSTI-based ART	1.8 (1.1-3.3)	0.046
Baseline HIV-1 RNA > 100,000 copies/ml	1.4 (0.8-2.4)	0.320
Female	1.1 (0.6-2.1)	0.690
IDU	1.3 (0.6-2.6)	0.510
Baseline BMI	1.3 (1.2-1.3)	< 0.001
Baseline CD4+ T cell count	1.0 (0.9-1.0)	0.220
CD4+ T cell count	1.0 (0.9-1.0)	0.850
CD8+ T cell count	1.0 (1.0-1.1)	0.052
Baseline CD4+/CD8+ T cell ratio	1.0 (0.3-3.2)	0.980
Age	1.0 (1.0-1.1)	0.530

Table 2. Multivariable Model for Factors Associated with SBP at 72 weeks post ART Initiation

Factor	Estimated difference in SBP (95% CI)	*p*-value
INSTI-based ART	6.6 (0.4-13.1)	0.048
Baseline HIV-1 RNA > 100000 copies/ml	0.6 (-5.8-6.9)	0.863
Female	12.0 (4.2-19.7)	0.003
History of Hypertension	-2.6 (-9.6-4.5)	0.473
IDU	8.0 (-0.7-16.7)	0.073
Baseline BMI	4.6*	0.032
Baseline CD4+ T cell count	1.0*	0.241
Age	1.0*	0.134



Conclusions: INSTI-based ART was associated in the short-term with a greater risk of overweight/obesity and SBP elevation. Patients developing overweight/obesity increased LDL cholesterol with no other metabolic disturbances.

Sesión de Comunicaciones Orales 2 - Jueves, 12 de diciembre, 10:15-12:15 h

OR-09. CONSECUENCIAS INMUNOLÓGICAS DE LA SIMPLIFICACIÓN A BITERAPIA (DTG/3TC O DRVC/3TC) EN PACIENTES CON TRIPLE TERAPIA BASADA EN INHIBIDORES DE LA INTEGRASA

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Introducción: Las simplificaciones a biterapias (BT) han demostrado una eficacia virológica similar a la triple terapia (TT). Sin embargo, no se conoce si puede tener consecuencias inmunológicas comparado con el mantenimiento de la TT.
Objetivos: Evaluar los efectos inmunológicos de la simplificación a BT en pacientes virológicamente suprimidos ≥ 1 año con TT basadas en inhibidores de la integrasa (II).
Métodos: Ensayo clínico independiente en el que pacientes con TT se aleatorizaron a continuar TT o simplificar DTG/3TC o DRVc/3TC. Se evaluó la evolución del cociente CD4/CD8, activación (HLADR/CD38), disfunción (PD-1), proliferación (Ki67), senescencia (CD57) y apoptosis (anexina V) en linfocitos $CD4^+$ y $CD8^+$. Asimismo, se midieron concentraciones plasmáticas de sCD14, TNF-α, IP-10, IL-6 y ADN proviral en PBMCs. Se compararon las diferencias entre las determinaciones basales y semana 48 entre los grupos (U de Mann Whitney).
Resultados: Se incluyeron 155 pacientes de los cuales 143 llegaron a semana 48 (1 fracaso virológico con DTG/3TC; 11 otros motivos). Hombres (91,6%), medianas de: edad 33 años (27-42), $CD4^+$ 756/µl (582-976) y tratamiento 38 meses (26-66). Tras 48 semanas no observamos cambios significativos en los parámetros inmunológicos entre DTG/3TC o DRVc/3TC (se analizan conjuntamente) ni entre estos y la TT.

Evolución de los parámetros inmunológicos. M (RIQ)

	TT (n = 51)		BT (n = 92)		*p*
	Basal	S48	Basal	S48	
$CD4^+/CD8^+$	0,9 (0,7-1,4)	1,1 (0,7-1,6)	0,8 (0,6-1,1)	1,0 (0,7-1,3)	0,334
$\%CD4^+HLADR^+CD38^+$	1,3 (1,1-1,8)	1,2 (0,9-1,7)	1,5 (1,2-1,9)	1,4 (1,1-2,2)	0,595
$\%CD4^+CD57^+CD28^-$	5,5 (1,8-11,9)	5,9 (2,6-19,0)	4,6 (2,1-8,7)	6,2 (2,2-12,6)	0,614
$\%CD4^+PD1^+$	7,1 (4,9-12,2)	6,5 (4,2-9,7)	8,8 (6,0-13,4)	6,8 (4,8-10,8)	0,369
$\%CD4^+Ki67^+$	0,7 (0,5-1,2)	0,8 (0,6-1,3)	0,9 (0,6-1,4)	0,9 (0,6-1,3)	0,951
$\%CD4^+Anexina^+$	0,6 (0,4-1,2)	1,0 (0,5-1,6)	0,8 (0,5-1,4)	1,0 (0,7-1,6)	0,646
sCD14 (µg/ml)	2,8 (2,1-3,6)	2,4 (1,9-3,6)	2,9 (2,2-3,6)	2,2 (1,7-3,3)	0,614
TNF-α (pg/ml)	0,9 (0,7-1,3)	1,1 (0,8-1,4)	0,99 (0,8-1,3)	1,06 (0,9-1,3)	0,721
IL-6 (pg/ml)	1,7 (1,3-2,3)	1,6 (1,1-2,7)	1,8 (1,1-2,9)	1,8 (1,3-3,1)	0,363
IP-10 (pg/ml)	83,0 (51,8-126,2)	89,4 (57,2-116,0)	91,7 (66,8-127,2)	90,7 (61,7-137,6)	0,642
ADN proviral (log copias/10^6 PBMCs)	2,7 (2,2-3,1)	2,6 (2,4-2,9)	2,7 (2,4-3,0)	2,7 (2,5-2,9)	0,615

Conclusiones: La simplificación a DTG/3TC o DRV/3TC es tan segura como la TT tanto desde el punto de vista virológico como inmunológico.

OR-10. ENV EL9 EPITOPE DRIVEN BY HLA B*1402 LEADS DISEASE PROGRESSION IN LTNP PATIENT AFTER TWENTY SEVEN YEARS OF HIV CONTROL

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Introduction: HIV control is associated to effective CD8+ T-cell cytotoxic (CTL) response directed against epitopes in *gag*. By the contrary, HLA-B*14:02 patients present an *env* immune-dominant response directed against the EL9 epitope (^{584}ERYLKDQQL^{592}). We performed a virological and immunologic longitudinal analysis of an HLA-B*14:02 LTNP (mean VL = 2,500 copies/ml), who lost viral control (VC) (≥ 10,000 copies/ml) after more than 27 years.
Methods: Viral sequences were obtained by limiting PCR from peripheral blood mononuclear cell (PBMCs) samples taken before or after the loss of VC. HIV evolution was analyzed estimating rates of synonymous and nonsynonymous diversity and divergence in *env* and *gag* regions. We explored amino-acid changes in the viral quasiespecies in two immune-dominant HLA-B*14:02 restricted epitopes: EL9 in *env* (^{584}ERYLKDQQL^{592}) and DA9 in *gag* (^{298}DRFYKTLRA^{306}). Two mutations L592R and K588R in EL9 were detected. We estimated the CTL response by IFNγ-ELISpot assay and by intracellular cytokine staining (ICS) in DA9 and EL9 peptides including the viral variants found L592R and K588R+L592R. Also, we constructed pseudo-viruses bearing L592R and L592R+ K588R mutations and evaluated its replicative capacity in TZM-bl cells.
Results: HIV evolution data suggested positive selection in *env* over time. Variability and emergence of HIV CTL mutations in EL9 *env* and DA9 *gag* were studied. No mutations in DA9 were observed. By contrast, the majority of viruses displayed a L592R mutation in the EL9 during the patient's follow-up. In addition, a second mutation in EL9, K588R appeared concomitant to the loss of VC and it became predominant in the last samples analyzed. CTL response showed an immune-dominant response to *env* EL9. IFNγ-ELISpot and ICS data demonstrated a lack of response against DA9 and a loss of response against EL9 over time linked to CTL mutational escape and selection of the K588R+L592R mutant. In addition, viral replicative capacity experiments indicated an increase by 6-fold (± 1.4) in replicative capacity by the L592R+ K588R double-mutant in relation to the L592R mutant.
Conclusions: Patient showed an immune-dominant response to EL9. Despite the dominant viral population displayed the escape mutant L592R, patient was able to control VL ≈2,500 copies/ml for 27 years. Loss of EL9 immune response was associated with the selection of the L592R+K588R variant with full replicative potential and associated with the loss of HIV control. These data suggested a strong contribution of *env* CTL immune responses to long-term HIV control and warrants its potential inclusion in novel CTL immunogens.

OR-11. AN ENVELOPED VIRUS-LIKE PARTICLE (VLP) PLATFORM WITH HIGH-DENSITY ANTIGEN DISPLAY INDUCES A STRONG HUMORAL IMMUNE RESPONSE

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Introduction and objectives: Human Immunodeficiency Virus-Like Particles (HIV-VLPs) are non-infectious, non-replicative and highly immunogenic Gag-based enveloped structures that mimic the virus' morphology. The HIV envelope glycoprotein (Env) is the main target of protective neutralising antibodies. An obstacle to induce potent humoral responses against HIV is the poor incorporation of Env into virions. The aim of the present work is to develop HIV-derived VLPs with a high density of Env-derived immunogens on their surface.
Methods: HIV-1 p55Gag was fused with a gp41-derived protein (Min) containing the Membrane Proximal External Region (MPER). VLPs were produced in HEK293F cells by transient transfection (Expi293 system). After 48 hours, supernatants were collected and VLPs (control-Gag and MinGag) were purified by centrifugation, crossflow filtration and HPLC. Protein expression was verified by flow cytometry, ELISA and western blot. VLP immunogenicity was assessed in C57bl/6 mice following two approaches: a) four doses of purified VLPs (VVVV; 90ng of p24/dose in PBS) and b) two doses of DNA (20μg of DNA in PBS) followed by two additional doses of purified VLPs (DDVV). DNA vaccination was performed *in vivo* by muscle electroporation. All immunisations were performed at 3-week intervals. The humoral response against Min and Gag proteins (total IgG and IgG-subclasses) was evaluated by ELISA. Neutralising activity of sera samples was evaluated *in vitro* by a TZM-bl-based neutralisation assay.
Results: Transfection of HEK293F cells with MinGag resulted in the proper expression of the fusion protein: Min domain was detected on the cell surface and Gag into the transfected cells. However, MPER presentation on VLP-producing cells strongly depended on the transmembrane and linker domains used to fuse both proteins. Immunogenicity results showed that MinGag-VLPs induced a robust antibody response in the VVVV group, reaching plateau after one immunisation. Interestingly, a 10-fold increase in anti-gag and anti-gp41 antibodies was achieved in the prime-boost regimen (DDVV). Non-neutralising activity was detected; however, anti-Min response was characterised by a strong bias to IgG2c, a Th1-like IgG subclass. In contrast, anti-gag response was more heterogeneous including IgG1, IgG2b and IgG2c antibodies.
Conclusions: We have generated a new HIV-based VLP platform that allows the incorporation of Env-derived immunogens at high density, increasing notoriously their immunogenicity and inducing antigen-specific Th1-like antibodies. In addition, the DNA-VLP prime-boost immunization strategy showed a better performance compared with the use of only VLPs. Further studies will assess the potential of these responses to generate an effector antibody-dependent protective response against HIV.

OR-12. PERSISTENT HIV-CONTROLLERS ARE MORE PRONE TO SPONTANEOUSLY CLEAR HCV

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Introduction: HIV-controllers have the ability to spontaneously maintain viremia at low or undetectable levels in absence of antiretroviral treatment. Furthermore, HIV controllers seem to have superior capacity to spontaneously clear hepatitis C virus (HCV) coinfection compared to non HIV-controllers. Some of these subjects eventually lose HIV-controller status, transient controllers, in contrast with HIV-controllers with persistent natural HIV control, persistent controllers. It is unknown whether persistent controllers have superior capacity to spontaneously clear HCV coinfection compared to transient controllers.
Methods: HIV-controllers with available data for antibodies to HCV (anti-HCV) were recruited (n = 744). Factors associated with HIV spontaneous control in relation to HCV coinfection were analyzed in persistent and transient HIV-controllers with anti-HCV positive (n = 202 and n = 138, respectively) in comparison with 1700 HCV coinfected non HIV-controllers. In addition, the factors related to the loss and time to lose HIV-controller status were explored (n = 744).
Results: A higher frequency of HCV spontaneous clearance was found in persistent HIV-controllers (25.5%) compared to non-controllers (10.2%). After adjusting for potential confounders as sex, age, HIV transmission risk, CD4+ T-cell nadir and time of follow up, HCV clearance was independently associated with persistent HIV spontaneous control (p = 0.002; OR (95%CI) = 2.573 (1.428-4.633), but not with transient spontaneous control (p = 0.119; 1.589 (0.888-2.845). Furthermore, persistent HIV-controllers were more likely to spontaneously clear the HCV in comparison with transient controllers (p = 0.027; 2.650 (1.119-6.276). Finally, no loss or a delayed time to lose HIV-controller status was independently associated with HCV spontaneous clearance (p = 0.010; 1.990 (1.177-3.364).
Conclusions: This study shows an association between spontaneous persistent HIV-control and HCV spontaneous clearance. Our results support the idea of common mechanisms implicated in spontaneous persistent HIV control and HCV clearance. These results highlight persistent HIV-controllers but not transient controllers as a good model of functional HIV cure.

OR-13. HIV/HCV COINFECTION IN SPAIN: TROUBLE WILL SOON BE OVER

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Objectives: We assessed the prevalence of anti-HCV antibodies (HCV-Ab) and active HCV infection (HCV-RNA-positive) in people living with HIV (PLWH) in Spain in 2018 and compared the results with similar studies performed in 2015, 2016, and 2017.
Methods: The study was performed in 43 centers (October-November 2018). The sample size was estimated for accuracy of 1.25%, the number of patients from each hospital was determined by proportional allocation, and patients were selected using simple random sampling. All oral DAA-based therapy has been available in Spain since the third trimester of 2014. Since June 2017, free access to treatment has been available to all HCV-infected individuals.
Results: The reference population comprised 40,650 PLWH (approximately 1/3rd of PLWH in Spain), and the sample size was 1,733. HCV serostatus was known in 1,721 (99.3%), and 578 (33.6%) were HCV Ab-positive (78.1% PWID and 10.9% MSM). Of these 578, 409 cleared HCV after anti-HCV therapy, 104 cleared HCV spontaneously, 64 were HCV-RNA-positive, and 1 had unknown HCV-RNA. The prevalence of HCV-RNA-positive was, therefore, 3.7%. As 21 of 64 patients were receiving DAAs, and assuming treatment effectiveness of 95%, the prevalence of HCV-RNA-positive could be considered to be 2.5%. A summary of the main findings in the four national cross-sectional studies is shown in the table. Overall, HCV-related liver cirrhosis was present in 6.6% of the PLWH, 10.9% of HCV-RNA-positives, and 26.4% of those who cleared HCV after anti-HCV therapy (p = 0.007).

Trends in HIV/HCV coinfection in Spain

	2015	2016	2017	2018	P trend
Centers - n	41	43	43	43	
Reference population - n	35,791	38,904	40,322	40,650	
Sample size - n	1,867	1,588	1,690	1,733	
Tested for HCV Ab -%	98.7	99.8	99.1	99.3	
HCV Ab-positive -%	37.7	34.6	34.0	33.6	
HCR-RNA positive -%	22.1	11.8	8.0	3.7	< 0.001
Anti-HCV treatment uptake -%	59.3	74.7	82.4	92.2	< 0.001

Conclusions: Active HCV infection among PLWH in Spain at the end of 2018 was 3.7%, that is, 83.3% lower than in 2015. Increased exposure to DAAs was the reason for this sharp decrease. The elimination of HCV infection among PLWH in Spain is an achievable goal shortly, but the burden of HCV-related cirrhosis will continue to be significant among these individuals.

OR-14. IMPACT OF SIGLEC-1 VARIANT ON DISSEMINATED TUBERCULOSIS DURING HIV-1 CO-INFECTION

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Naturally occurring null individuals lacking functional alleles facilitate the study of particular genes during infectious diseases. We previously described a loss-of-function variant on the myeloid-cell surface receptor Siglec-1/CD169 that mediates HIV-1 capture and infection of $CD4^+$ T cells. Here we investigated the effect of Siglec-1 truncation on HIV-1 related co-infections in two large cohorts comprising 6,200 individuals, in which we found a significant association between extrapulmonary dissemination of *Mycobacterium tuberculosis* (Mtb) and the Siglec-1 variant. The association of the Siglec-1 null allele on HIV-1 related co-infections was studied in the Swiss HIV Cohort Study (SHCS). Results were further confirmed in an independent Russian cohort of individuals with tuberculosis (TB). Functional implications were assessed in a murine and a cellular model lacking Siglec-1 expression. The ability of Mtb to directly interact with Siglec-1 was tested by cellular assays and thin-layer chromatography. The capacity of Siglec-1 on antigen presenting cells (APCs) to trap extracellular vesicles (EVs) derived from Mtb-infected cells was measured by FACS, microscopy and ELISpot. We found a significant association between Mtb and the Siglec-1 null variant in the two cohorts, which was linked to an extra-pulmonary dissemination of the bacteria (proportion test or hypergeometric test, according to the cohort's design, $p < 0.02$). Mtb dissemination was also evident in Mtb-infected Siglec-1 knockout mice, which had larger pulmonary damage as compared to wild type mice (Mann-Whitney U-test, $p < 0.03$). This could not be attributed to a reduced clearance of Mtb via Siglec-1. However, we found that Siglec-1 was necessary to induce antigen presentation via EV uptake, as EVs produced on Mtb-infected cells were captured by APCs, and this uptake was blocked by an anti-Siglec-1 mAb (one sample t-test, $p < 0.0094$). Importantly, only APCs capturing EVs via Siglec-1 triggered IFN-γ production on autologous PBMCs. The absence of Siglec-1 may delay the onset of immunity against Mtb, facilitating an early dissemination of Mtb in HIV-1 co-infected individuals. Research suggests that the Siglec-1 might help protecting against disseminated tuberculosis while might also play a deleterious role in enhancing trans-infection of HIV-1, exemplifying the biological phenomenon known as antagonistic pleiotropy.

OR-15. VIROLOGICAL CHARACTERIZATION IN YOUTH HIV-DIAGNOSED DURING ADOLESCENCE IN SPAIN IN THE 1980-2017 PERIOD

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Introduction: Young people accounted for over 30% of all new HIV infection globally. There are scarce reports focused on virological status in adolescents and no data of Spanish adolescents has been published. Characterization of newly HIV-1 infected adolescents could help to define and improve their follow-up needs in units (pediatrics and adults).
Objectives: To describe virological outcome of adolescents with a HIV diagnosis between 12 and 20 years age in Spain from 1980 to 2017.
Methods: Retrospective multicenter study performed in HIV-1 adolescent diagnosed between 12 and 20 years age in Spain until December 2017, with available resistance *pol* genotypes enrolled in the Spanish Paediatric HIV Cohort (CoRISpe) or the Spanish adult cohort of HIV-infected patients (CoRIS). We analyzed demographical and

clinical features such as viral load, CD4 counts at diagnosis and sampling time, prevalence of transmitted (TDR).

Results: Among 357 HIV-1 adolescents diagnosed between 12 and 20 years-old in Spain, 122 had information about resistance. These 122 adolescents were diagnosed when they were 12-14 years (5.7%), 15-17 years (18.9%) o 18-20 years (75.4%) being enrolled at CoRIS (88.5%) or CoRISpe (11.5%) cohorts. They were mostly male (83.6%), Spanish (57.4%) and with high viral load (median 4.5 log) and CD4 counts (median 508) at diagnosis. The way of transmission was mainly behaviorally (88.5%): men who have sex with men, MSM (59.8%), heterosexual (21.3%), or drug users (7.4%). A 5.7% were transfusion receivers and 3.7% from vertical transmission. Around one third (29%) of newly diagnosed adolescents were late presenters (< 350 CD4 counts/μl or AIDS at diagnosis). We found a significant higher rate of late presenters among heterosexually HIV-infected vs. MSM (38% vs. 21%; $p < 0.05$) even the highest rate was among vertically infected (100%). Among the 112 (31.4%) HIV-1 infected during the adolescence with available *pol* sequences, the 81.9% were treatment-naïve at sampling. The prevalence of transmitted drug resistance (TDR) was 18%: 15% for NNRTIs, 2% for NRTIs and 1.4% for PI. The most prevalent TDR mutation was the E138A resistance mutation to NNRTI class drugs.

Conclusions: Our data suggest a high TDR prevalence among adolescents diagnosed between 12 to 20 years, even if they acquire HIV manly from behaviorally transmission and being mostly naïve at sampling. This could have implications for choosing initial regimens for ART-naïve adolescents.

OR-16. HIV CONTINUUM OF CARE BY SEX AND MODE OF TRANSMISSION IN SPAIN, 2016: USE OF DIFFERENT SOURCES OF INFORMATION

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Objectives: Our aim was to calculate the HIV Continuum of Care (CoC) by sex and mode of transmission in Spain, 2016.

Methods: Stage 1: People living with VIH (PLHIV) and stage 2: PLHIV diagnosed were estimated using mathematical models based on surveillance data (*New HIV diagnoses and AIDS cases Information Systems). Stage 3:* Diagnosed PLHIV on ART and stage 4: PLHIV on ART with viral load suppressed (VLSUP) were calculated using both cohort data - *multicenter cohort of HIV-infected adults of the Spanish HIV/AIDS Research Network (CoRIS)* and cross-sectional data - *one-day cross-sectional hospitals survey.* The four stages were estimated stratifying by sex and mode of transmission.

Results: The overall HIV prevalence was 0.37%, 0.62% in men and 0.13% in women. Table 1 summarizes the estimates for the four stages of the HIV Continuum of Care by sex and mode of transmission. The global percentage of PLHIV with viral load suppressed varied from 69.0% using cohort data to 72.8% using cross-sectional data in Spain. These percentages varied from 69.6% to 71.3% for men and from 65.7% to 76.4% for women using cohort or cross-sectional data, respectively. Likewise, these figures ranged between 68.7% and 70.7% for men who had sex with men (MSM); 66.8% and 84.9% for persons who inject drugs (PWID) and between 64.9% and 69.9% for heterosexuals using cohort or cross-sectional data, respectively.

Conclusions: Spain is very close to achieve the global UNAIDS goal (73% of PLVIH virally suppressed). In our complex epidemic, there is a need to assess gaps in the different subpopulations for guiding specific prevention strategies. The use of different data sources lets us a better approach to the current situation of HIV infection in Spain.

Table 1. Estimates for the four stages of the HIV Continuum of Care by sex and mode of transmission in Spain, 2016

	PLHIV	PLHIV Diagnosed	On ART		VLSUP	
			Cross-sectional data	Cohort data	Cross-sectional data	Cohort data
	N	%	%	%	%	%
Global	146,500	86.2	93.4	92.5	90.4	86.5
Sex						
Male	119,937	86.2	92.4	92.5	89.6	87.3
Female	26,559	86.3	96.0	92.2	92.3	82.6
Mode of transmission						
MSM	58,936	83.5	92.0	92.9	92.0	88.6
PWID	20,278	97.6	93.5	86.4	93.0	79.2
Heterosexual	30,404	82.9	94.9	93.3	88.8	83.9