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Comunicaciones Orales

# VII Congreso Nacional de GESIDA y 9.ª Reunión Docente de la RIS

Madrid, 1-4 de diciembre de 2015

## Miércoles, 2 de diciembre. Sala Auditorio (08:30-10:30 h)

### CO-01. HIGH EFFICACY OF GRAZOPREVIR/ELBASVIR IN HCV GENOTYPE 1, 4, AND 6-INFECTED PATIENTS WITH HIV CO-INFECTION: THE PHASE 3 C-EDGE CO-INFECTION STUDY

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**Background and objective:** The fixed-dose combination of grazoprevir (GZR, MK-5172, 100 mg, an NS3/4 protease inhibitor)/elbasvir (EBR, MK-8742, 50 mg, an NS5A inhibitor), an interferon-free, ribavirin-free, once-daily tablet has shown robust efficacy and safety in diverse populations. C-EDGE Co-infection is an on-going phase-III study evaluating GZR/EBR among treatment-naive, HIV/HCV co-infected patients with HCV genotype (GT) 1, 4, or 6 infection.

**Methods:** Enrolled patients were on a stable antiretroviral (ARV) regimen (tenofovir or abacavir, and lamivudine or emtricitabine; and either raltegravir, dolutegravir or rilpivirine) with a CD4 cell count > 200 cells/mm$^3$ and an HIV RNA viral load < 20 copies/mL, or were HIV treatment-naive with CD4 cell count > 500 cells/mm$^3$ and HIV RNA viral load < 50,000 copies/mL. All patients received open-label GZR/EBR for 12 weeks. The primary efficacy endpoint was sustained virologic response at follow-up week 12 (SVR12). All patients underwent testing for HCV resistance associated variants (RAVs) at baseline, and at failure and follow-up in those with virologic failure. Phylogenetic analysis was performed to distinguish relapse from reinfection.

**Results:** 218 patients were enrolled. In the Full Analysis Set population (all patients who received ≥ 1 dose of study medication), SVR12 was achieved by 210/218 (96.3%) patients, including 35/35 (100%) patients with cirrhosis, 34/36 (94.7%) of African Americans, and 121/127 (95.3%) of patients with baseline HCV RNA > 800,000 IU/mL. 5/218 (2.3%) patients failed to clear HCV infection that was present pre-therapy. Of the 5 virologic relapses, two had baseline NS5A RAVs with > 5x resistance to EBR *in vitro* (L31M, Y93S). Adverse events (AEs) were reported in 157/218 (72%) patients; serious AEs occurred in 2/218 (0.9%) patients. Adherence was > 90% in the total population, including virologic failures.

**Conclusions:** A 12-week regimen of GZR/EBR fixed-dose combination was highly effective among HIV/HCV co-infected patients with GT1, 4 or 6 infection, with a favorable safety profile. SVR was high across all patient subgroups including African-Americans and those with cirrhosis.

**Table CO-01.** SVR12 by Genotype

| | All patients | GT1a | GT1b | GT4 |
|---|---|---|---|---|
| | (N = 218) | (N = 144) | (N = 44) | (N = 28) |
| SVR12* | | | | |
| n/N | 210/218 | 139/144 | 42/44 | 27/28 |
| % | 96.3% | 96.5% | 95.5% | 96.4% |
| 95%CI | 93.5, 98.7 | 92.1, 98.9 | 84.5, 99.4 | 81.7, 99.9 |
| LTFU or unrelated to VF | 1 | 0 | 1 | 0 |
| Relapse | 5 | 4 | 0 | 1 |
| Reinfection | 2 | 1 | 1 | 0 |

*HCV RNA assessed via COBAS TaqMan v2.0 [lower limit of quantitation <15 IU/mL]
N = Number of subjects included in the analysis.
n (%) = Number of subjects who achieved SVR12 and the percentage calculated as (n/N)*100.

### CO-02. HIV-1-RNA DECAY AND DOLUTEGRAVIR CONCENTRATIONS IN SEMEN OF PATIENTS INITIATING A FIRST ANTIRETROVIRAL REGIMEN

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**Objective:** To quantify HIV-1 RNA decay and dolutegravir (DTG) concentrations in semen of HIV-1 infected patients initiating antiretroviral therapy (ART) with DTG plus abacavir/lamivudine (ABC/3TC).

**Methods:** Prospective, single-arm, open-label study including 15 HIV-1 infected, ART-naïve men initiating DTG+ABC/3TC. HIV-1 RNA was measured in paired seminal (SP) and blood plasma (BP) samples at baseline, days 3, 7, and 14, and weeks 4, 12 and 24. The HIV-1 RNA decay rate in plasma and seminal fluid was assessed using nonlinear

mixed-effects models. Total DTG concentration at the end of the dosing interval ($C_{24h}$) was quantified in in SP and BP at weeks 4 and 24 by a validated LC-MS/MS method.
**Results:** Patient characteristics at baseline were: Median (range) age 35 (22-60) years; CD4+ cell count 504 (60-782) cells/µL; BP HIV-1 RNA 5.03 (4.02-5.76) log copies/mL; SP HIV-1 RNA 3.91 (2.97-4.82) log copies/mL; and HIV-1 subtype B and non-B in 11 and 4 patients, respectively, with no differences in median HIV-1 RNA in BP and SP according to B or non-B HIV-1 subtype. Viral decay was faster in BP than in SP in the first decay phase (half-life 4.5 vs 8.6 days, p = 0.0001) but differences in the second decay phase were not statistically significant (54 vs 156 days, p = 0.43). Median time to HIV-1 RNA < 40 copies/mL was significantly shorter in SP than BP (4 vs 12 weeks, p = 0.008) with no differences when adjusted by baseline HIV-1 RNA. Overall, median DTG $C_{24}$ in SP was 119.1 (27.2-377) ng/mL, which was 7.8% (3.7-21%) of the BP $C_{24}$. The lowest seminal DTG concentration observed was 78-fold the *in vitro* $IC_{50}$ (0.2 ng/mL).
**Conclusions:** Although the DTG concentration in SP was only 7.8% of the BP concentration, it sufficed to contribute to achieving rapid suppression of HIV-1 replication in this compartment.

## CO-03. CHANGES IN RENAL LABORATORY PARAMETERS AND BONE MINERAL DENSITY IN TREATMENT-NAÏVE HIV-1- INFECTED ADOLESCENTS INITIATING THERAPY WITH INSTI-BASED SINGLE-TABLET REGIMENS CONTAINING TENOFOVIR ALAFENAMIDE (TAF) OR TENOFOVIR DISOPROXIL FUMARATE (TDF)

E. Negredo[1], A. Gaur[2], H. Kizito[3], W. Prasitsuebsai[4], N. Rakhmanina[5], K. Chokephaibulkit[6], J. Fourie[7], L.G. Bekker[8], Y. Shao[9], S. Bennett[9], E.M. Xicola[10] and E. Quirk[9]

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**Background:** EVG/COBI/FTC/TAF [E/C/F/TAF] and EVG/COBI/FTC/TDF [Stribild, STB] are integrase inhibitor (INSTI)- based single-tablet regimens (STRs) in clinical development for HIV-1-infected adolescents. Exposures of all components have been shown to be within the range associated with antiviral activity in adults. Preliminary comparative safety data through 24 weeks are reported.
**Methods:** Treatment-naïve 12 to < 18 year-olds weighing ≥ 35 kg with HIV-1 RNA > 1000 copies/mL, CD4 >100 cells/µL and eGFR > 90 mL/min/1.73 $m^2$ received E/C/F/TAF or STB once daily in two ongoing 48-week, single-arm, openlabel trials. Adverse events (AE), laboratory tests, bone mineral density (BMD) by dual X-ray absorptiometry and height-age adjusted (HA) Z-scores were assessed through Week 24.
**Results:** The E/C/F/TAF and STB trials enrolled 50 and 33 adolescents, respectively (median age 15 vs 16 years, 56% vs 30% female, 88% vs 76% Black, 22% vs 27% with baseline HIV-1 RNA > 100,000 copies/mL, median CD4 count 456 vs 407 cells/µL, median eGFR 156 vs 143 mL/min/1.73 $m^2$). Most AEs in both trials were mild and unrelated to treatment, with no deaths or AEs leading to treatment discontinuation. At Week 24, the median increase in serum creatinine was +0.08 mg/dL in E/C/F/TAF participants, with and +0.10 mg/dL in STB participants, with median eGFR decreases of -17.0 and -18.0 mL/min/1.73 $m^2$, respectively, consistent with COBI's inhibition of renal tubular creatinine secretion. Proteinuria (any grade) occurred in 26% of E/C/F/TAF participants vs 52% of STB participants, with Grade 2 or higher proteinuria occurring in 4% vs 21% of participants, respectively. Of those participants with BMD measurements at Week 24, the median increase in spine BMD was +1.98% in E/C/F/TAF participants, with a decrease of ≥ 4% in 3/41 participants (7%), versus a median decrease of -1.29% in the STB cohort, with a decrease of ≥ 4% in 6/20 participants (30%). Spine HA Z-scores decreased by -0.02 and -0.21 respectively.
**Conclusions:** Compared with STB, E/C/F/TAF exhibited similar effects on eGFR, a lower incidence and severity of proteinuria, and a median increase in spine mineralization. Both STRs were well-tolerated through 24 weeks. These findings support INSTI-based STRs as initial HIV-1 treatment in adolescents and suggest that TAF could offer safety advantages in pediatric populations.

## CO-04. SCREENING OF SEVERAL POLYANIONIC CARBOSILANE DENDRIMERS WITH ANTIVIRAL ACTIVITY AGAINST HEPATITIS C VIRUS BY INHIBITING VIRUS ENTRY IN A CELL CULTURE SYSTEM

D. Sepúlveda Crespo[1], P.L. Majano[2], R. Gómez[3], F.J. de La Mata[3], J.L. Jiménez[1], M.A. Muñoz-Fernández[1] and P. Gastaminza[4]

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**Background:** Hepatitis C virus (HCV) is the major cause of acute and chronic liver disease, cirrhosis, hepatocellular carcinoma and liver failure. Although new direct antiviral agents (DAAs) have been successfully developed for the treatment of chronic HCV infection, resistance to these DAAs has been shown to emerge rapidly in clinic. Therefore, the development of novel agents is urgently needed. The area of entry of HCV into hepatocytes and entry inhibitors are largely unexplored. HCV entry into cells represents a promising target for novel antiviral strategies to prevent virus/receptor interactions and to interfere with virus/cell membrane fusion. Polyanionic carbosilane dendrimers (PCDs) have demonstrated potent and broad-spectrum anti-HIV/HSV-2 activity *in vitro* and *in vivo*. However, the potential anti-HCV effect of PCDs has not been completely probed.
**Methods:** We used an unbiased, cell-based system to screen a battery of PCDs aiming at identifying non-toxic antiviral compounds targeting different steps of the HCV lifecycle. We selected the PCDs displaying the best 7 selectivity indexes against 2a HCV particles produced in cell culture (HCVcc). Moreover, to further characterize them by determining the genotype spectrum and step targeted in the HCV lifecycle, we also used genotypes 1a and 1b HCVcc, trans-complemented, spread-defective HCV virions (HCVtcp) and HCV pseudotyped retroviral particles (HCVpp).
**Results:** Our results show that PCDs inhibit infection by genotypes 1a, 1b, and 2a HCVcc, genotype 2a HCVtcp and HCVpp of the major genotypes at nanomolar concentrations with no associated cellular toxicity affecting early steps of the HCV lifecycle. Interestingly, while exposure to most compounds did not alter virion infectivity, one of the PCDs irreversibly destabilized infectious virions, making infectivity undetectable and strongly reducing viral RNA integrity, even after PCD removal.
**Conclusions:** In summary, PCDs are identified as novel anti-HCV agents that target either the virion itself or early aspects of HCV infection. This system provides an efficient and cost-effective screen for compounds with antiviral activity against HCV and constitutes a step forward in the development of PCDs as nanotools to prevent HCV transmission in humans.

## CO-05. IMPLICACIÓN DEL MIRNA-33 EN EL EFLUJO DE COLESTEROL MEDIADO POR ABCA1 EN MACRÓFAGOS INFECTADOS POR VIH

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**Objetivo:** La infección por el VIH está asociada con la alteración de elementos locales y sistémicos del transporte reverso del colesterol, incluyendo el eflujo del colesterol (EC), el cual juega un papel importante en el mantenimiento de la homeostasis celular. La proteína viral Nef inhibe la actividad del receptor de membrana *ATP-binding cassette sub-family A member 1* (ABCA1) y su consiguiente función de EC. La inhibición de ABCA1 está regulada a nivel post-transcripcional por el microRNA (miRNA)-33. El objetivo de este estudio fue indagar si miRNA-33 regula ABCA1 en macrófagos infectados con VIH.
**Metodología:** Se infectaron células THP1 diferenciadas a macrófagos (THP1d) con los virus AD8WT y AD8ΔNef (ambos con tropismo para R5). Transcurrida una semana de infección se procedió a la transfección con anti-miRNA-33 y mimic-33 usando *Lipofectamina* durante 48 h. Para las medidas de EC, se cargaron las células con colesterol-[$H^3$] y se analizó el eflujo mediante ensayo de radioactividad a día 9 posterior a la infección. Los niveles de ABCA1 fueron evaluados mediante RT-qPCR y western-blot.
**Resultados:** Después de 48 h de transfección con anti-miRNA-33, se observó un ligero incremento en la expresión de ABCA1 en las células THP1d sin infectar. Los niveles de EC disminuyeron en las células THP-1 infectadas con el virus AD8 pero se mantuvieron en las infectadas con el virus AD8ΔNef. Los niveles de proteína ABCA1 disminuyeron en las células infectadas y transfectadas con antimiR-33 respecto a su control sin virus. Sin embargo, no se detectaron diferencias en los niveles de proteína ABCA1 en función del virus utilizado para la infección (AD8WT o AD8ΔNef). Tampoco se observaron diferencias en la expresión génica de ABCA1.
**Conclusiones:** La expresión de ABCA1 está alterada independientemente por miRNA-33 y VIH a nivel post-transcripcional. No se observaron cambios de expresión de ABCA1 en la transfección de anti-miRNA-33 en células infectadas por AD8WT o AD8ΔNef aunque Nef está implicado en el EC. Esto sugiere que la proteína viral Nef juega un papel fundamental en el metabolismo del colesterol e independiente a la expresión de ABCA1.

## CO-06. THE HDAC6/APOBEC3G COMPLEX REGULATES HIV-1 INFECTIVENESS BY INDUCING VIF AUTOPHAGIC DEGRADATION

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**Background:** Human immunodeficiency virus type 1 (HIV-1) has evolved a complex strategy to overcome the immune barriers it encounters throughout an organism thanks to its viral infectivity factor (Vif), a key protein for HIV-1 infectivity and in vivo pathogenesis. Vif interacts with and promotes "apolipoprotein B mRNA-editing enzyme-catalytic, polypeptide-like 3G" (A3G) ubiquitination and subsequent degradation by the proteasome, thus eluding A3G restriction activity against HIV-1.
**Results:** We found that cellular histone deacetylase 6 (HDAC6) directly interacts with A3G through its C-terminal BUZ domain (residues 841–1,215) to undergo a cellular co-distribution along microtubules and cytoplasm. The HDAC6/A3G complex occurs in the absence or presence of Vif, competes for Vif-mediated A3G degradation, and accounts for A3G steady-state expression level. In fact, HDAC6 directly interacts with and promotes Vif autophagic clearance, thanks to its C-terminal BUZ domain, a process requiring the deacetylase activity of HDAC6. HDAC6 degrades Vif without affecting the core binding factor β (CBF-β), a Vif-associated partner reported to be key for Vif- mediated A3G degradation. Thus HDAC6 antagonizes the proviral activity of Vif/CBF-β-associated complex by targeting Vif and stabilizing A3G. Finally, in cells producing virions, we observed a clear-cut correlation between the ability of HDAC6 to degrade Vif and to restore A3G expression, suggesting that HDAC6 controls the amount of Vif incorporated into nascent virions and the ability of HIV-1 particles of being infectious. This effect seems independent on the presence of A3G inside virions and on viral tropism.
**Conclusions:** Our study identifies for the first time a new cellular complex, HDAC6/A3G, involved in the autophagic degradation of Vif, and suggests that HDAC6 represents a new antiviral factor capable of controlling HIV-1 infectiveness by counteracting Vif and its functions.

## CO-07. IMPACT OF LATE PRESENTATION ON SHORT, MID AND LONG-TERM MORTALITY AND ON CAUSES OF DEATH IN SPAIN (2004-2013)

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**Objective:** To describe trends and risk factors for late presentation (LP) in the decade 2004-2013, and to analyze the impact on global mortality and the causes of death.
**Methods:** We analyzed data from a nation-wide cohort in Spain. LP was defined as having AIDS or CD4 < 350 cells/ml at the time of HIV diagnosis. Multivariate Cox models were used to estimate the effect on mortality and multivariate logistic regression to analyze trends and associated factors.
**Results:** Of 7,165 new HIV diagnoses, 46.9% were LP ($CI_{95\%}$:45.7-48.0). LP fell from 55.9% in 2004-05 to 39.4% in 2012-13, and was reduced 46.1% in men who have sex with men (MSM) and 37.6% in heterosexual men (HTX-men), but increased by 22.6% in HTX-women. Related risk factors with LP are shown in the table. There were 240 deaths, with a cause identified in 207 (86%). Global mortality was 1.01/100 py ($CI_{95\%}$:0.9-1.1). In the first year after diagnosis and compared to non-LP, mortality was 10 times higher in LP $aHR_{LP.vs.nLP}$ = 10.3 ($CI_{95\%}$: 5.5-19.3) and 23 times higher in subjects with AIDS at diagnosis $HR_{AIDS.vs.nLP}$ = 22.6 ($CI_{95\%}$: 11.5-44.6). Between 1-4 years since diagnosis, $aHR_{LP.vs.nLP}$ = 1.9 (1.2-3.0); and, > 4 years, $aHR_{LP.vs.nLP}$ = 1.5 (0.7-3.1). Causes of death during the first year after diagnosis were: HIV/AIDS (globally: 73%; 75%-LPvs40%-nLP; p < 0.013); liver-related (9%;8%-LP. vs 40%-nLP), malignancies (7%; 7%-LPvs.20%-nLP), and other infectious diseases (6%;6-LP. vs 0%-nLP). Over 4 years, malignancies (32%; 39%-LP. vs 14%-nLP), liver-related (20%; 22%-LP. vs 14%-nLP), HIV/AIDS (16%; 17%-LP. vs 14%-nLP) and other infections (16%; 17%-LP. vs 14%-nLP).
**Conclusions:** Despite a significant reduction in the last decade, LP continues to be an important problem especially among low educated, non-Spanish and HTX-women. LP is associated with higher mor-

tality, especially short-term mortality and due to HIV/AIDS. Mid-term mortality remained also higher in LP than nLP but no differences were observed in long-term mortality. Malignancies were the main cause of death among patients who survived > 4 years.

**Table CO-07.** Related risk factors associated with late presentation

| | | % LP | OR | CI 95% |
|---|---|---|---|---|
| Sex | Women | 55.2 | 1 | |
| | Men | 45.0 | 1.4 | 1.2-1.7 |
| Age (years) | ≤ 30 | 34.9 | 1 | |
| | 31-40 | 46.9 | 1.6 | 1.4-1.8 |
| | 41-50 | 57.1 | 2.2 | 1.8-2.6 |
| | > 50 | 69.2 | 3.6 | 2.9-4.4 |
| Category of transmission | MSM | 36.7 | 1 | |
| | IDUs | 64.9 | 2.8 | 2.0-3.8 |
| | Heterosexual | 59.3 | 2.2 | 1.7-3.0 |
| Educational level | Primary | 61.8 | 1.5 | 1.1-2.0 |
| | Lower Secondary | 55.3 | 1.3 | 1.1-1.5 |
| | Upper Secondary | 42.1 | 1.0 | 0.9-1.2 |
| | University | 37.8 | 1 | |
| Region of origin | Spain | 45.0 | 1 | |
| | Sub Saharan Africa | 63.8 | 1.6 | 1.3-2.0 |
| | Latin America | 49.3 | 1.4 | 1.2-1.8 |

## CO-08. ADQUISICIÓN DE VIH EN INMIGRANTES QUE VIVEN EN EUROPA: RESULTADOS DEL ESTUDIO AMASE (AVANZANDO EN EL ACCESO DE LOS INMIGRANTES A LOS SERVICIOS DE SALUD EN EUROPA)

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**Objetivo:** Evaluar si la adquisición del VIH en inmigrantes tuvo lugar antes o después de la migración a uno de los nueve países de la UE que participan en el estudio aMASE.
**Métodos:** El cuestionario fue diseñado por la red europea Eurocoord y cumplimentado en las consultas de VIH. La entrevista fue administrada en ordenador/*tablet* y completada por 1.784 personas diagnosticadas de VIH en los últimos 5 años, mayores de edad, nacidas fuera del país en que participan en el estudio y capaces de completar la encuesta en alguno de los 15 idiomas disponibles. Se entrevistó a personas en Bélgica (191), Alemania (31), Grecia (166), Italia (43), Holanda (84), Portugal (124), España (635), Suiza (133) y Reino Unido (377). El estudio se realizó entre julio de 2013 y julio de 2015. Las preguntas cubrían aspectos epidemiológicos, socio-económicos, clínicos, comportamentales y sobre la trayectoria migratoria que fue complementada con información clínica sobre serología previa de VIH, determinaciones de CD4, carga viral y subtipo viral. El momento de adquisición del VIH fue asignado en base a la historia de serologías de VIH y a la información sobre comportamientos de riesgo. La evidencia completa de adquisición post-migración se consideró en caso de una prueba negativa después de la migración antes de la positiva.
**Resultados:** De 1.784 sujetos, 1.207 tenían información sobre prueba de VIH previa y/o sobre comportamientos de riesgo: 703 tenían un test de VIH negativo en los tres años previos al test positivo, 532 no tenían información para la asignación directa del momento de adquisición. La adquisición post-migración con evidencia completa o probable fue más elevada entre los hombres que tienen sexo con hombres (HSH) (72%) que en heterosexuales (38%) y en las personas de Europa Occidental (72%), Central (58%), y del Este (58%) y de América Latina (68%), en los que las proporciones de HSH son más elevadas, que en los subsaharianos (SS) (32%). La adquisición pre-migración fue más elevada entre SS (20%) aunque en el 48% de los casos no fue posible establecer directamente el momento de adquisición de VIH.
**Conclusiones:** Una proporción alta de los inmigrantes con VIH que viven en Europa, especialmente entre los HSH, adquirieron el VIH después de la migración, por lo que es necesario diseñar intervenciones específicas. En una importante proporción de SS no se pudo asignar directamente el lugar de adquisición del VIH y se están desarrollando modelos más complejos de asignación.

## CO-09. INCIDENCE OF DE NOVO MALIGNANCIES IN HIV-INFECTED LIVER TRANSPLANT RECIPIENTS

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**Background:** Liver transplant (LT) recipients have a greater risk of *de novo* malignancy and of malignancy-related death than the age- and sex-matched general population. HIV-infected patients also have an increased risk of malignancy. However, it is unknown whether HIV infection further increases the risk of malignancy after LT. The aim of the study was to assess the incidence and clinical characteristics of *de novo* tumors in HIV-infected LT recipients.
**Methods:** This investigation consisted of a national multicenter cohort study including 271 consecutive adult patients with HIV infection who underwent LT between 2002 and 2012 in Spain (FIPSE cohort) and were prospectively followed until July 2014. These patients were matched with 813 non–HIV-infected LT recipients (1:3) for center, calendar year of LT (± 1 year), age (± 12 years), gender, liver disease etiology, and presence of hepatocellular carcinoma (HCC). All tumors, except HCC recurrence and non-melanoma skin cancers, after LT were considered events for this study.
**Results:** After a median (IQR) follow-up of 53 (24-78) months, 56 recipients (5%) developed *de novo* tumors: 15 recipients with HIV infection (5%) and 41 non–HIV-infected recipients (5%) ($p$ = 0.76). The most frequently diagnosed types of tumor were Non-Hodgkin lymphoma (n = 14), lung cancer (n = 10), and gastrointestinal cancer (n = 7). Time of onset, distribution, and tumor stage at diagnosis were similar in both groups. Among HIV-infected individuals, the median (IQR) CD4+ T cell count at de *novo tumor* diagnosis was 318 (171-543) cells/mm$^3$, and 93% had a plasma HIV RNA level below 50 copies/mL on antiretroviral therapy. The incidence rate of *de novo* tumors at 3, 5, and 7 years was, respectively, 4.3% (2.3-8.1%), 7.2% (4.2-12.2%), and 7.2% (4.2-12.2%) in HIV-infected patients and 3.1% (2.1-4.7%), 6.2% (4.4-8.6%), and 7.3% (5.2-10.00%) in non–HIV-infected patients. Survival rates at 1 and 3 years after the diagnosis of a *de novo* tumor were 34% (95%CI, 20-50) and 25% (95%CI, 20-50) in non–HIV-infected patients and 53% (95%CI, 26-74) and 44% (95%CI, 19-68) in HIV-infected recipients ($p$ = 0.179).

**Conclusions:** HIV-infected liver recipients do not have a greater mid-term risk of malignancy than non–HIV-infected liver recipients. The type of *de novo* tumor, the time of onset, and stage at diagnosis were similar in both groups.

### CO-10. SITUACIÓN CLÍNICA DE PACIENTES COINFECTADOS VIH-VHC VS MONOINFECTADOS VIH DE TRANSMISIÓN VERTICAL EN EL MOMENTO DEL PASO A UNIDADES DE ADULTOS

C. Fernández Mcphee[1], T. Sáinz[2], S. Jiménez[1], M.J. Mellado[2], T. Noguera[3], P. Soler[4], A. Pérez[5], A. Piqueras[5], L. Escosa[2], A. Mur[6], M. Coll[7], T. Vallmanya[8], J. Couceiro[9], I. Pocheville[10], J.A. León[11], J.T. Ramos[12], M. García-Hortelano[13], M.I. González-Tomé[14], M.L. Navarro[1] y Grupo de Trabajo CoRISpe[1]

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**Antecedentes:** En niños la infección por VHC es poco sintomática pero no se conoce bien la evolución del VHC en presencia del VIH. Una vez alcanzada la adolescencia, estos pacientes se transfieren a unidades de adultos. Este estudio pretende comparar el estado clínico de los pacientes VIH *vs* VIH-VHC en el momento del paso a adultos.
**Métodos:** Estudio transversal, se incluyen pacientes VIH y VIH-VHC de transmisión vertical registrados en CoRISpe que han sido transferidos a las unidades de adultos antes de diciembre de 2014.
**Resultados:** En el punto de corte, 444 (39,7%) pacientes infectados por TV registrados en CoRISpe habían sido transferidos a unidades de adultos, de los cuales 56 (12,6%) estaban coinfectados. Se comparó el grupo de pacientes VIH-VHC con pacientes VIH y, en ambos grupos, la proporción de mujeres era similar (55,3 vs 55,7%). No se observaron diferencias en la edad en el momento de transición (18 [16,8-18,8] vs 18,1 [16,8-19,1], p = 0,6), ni en el nadir de %CD4 (12,7% [7-19%] vs 13% [6-19%], p = 0,7) ni en el número de pautas de TAR recibidas (5,6 vs 5,8, p = 0,7). En un análisis por periodos (2005-2009 y 2010-2014) se observó que ambos grupos de pacientes presentan buenos CD4: 680 cel/mm$^3$ [370-916] vs 629 cel/mm$^3$ [428-862] (p = 0,74) en el primer periodo y 730 cel/mm$^3$ [598-882] vs 807,5 cel/mm$^3$ [533-1014] (p = 0,4) en el segundo, aunque la tendencia muestra un mejor control virológico (VIH-ARN < 50 cop/mL) en ambos periodos por parte de los pacientes VIH-VHC (52,4 vs 44,7% y 64 vs 58,8%); además, había menos proporción de casos de SIDA en los pacientes VIH-VHC (13 vs 27,2% y 12 vs 28,8%). El número de coinfectados sin TAR era menor y nulo: 8,7 vs 16,5% y 0 vs 7,5% y en mayor porcentaje recibían pautas QD: 17,4 vs 12,6% y 48 vs 35%. Un tercio de los pacientes VIH-VHC pasaron a adultos en un estado de fibrosis F0-1 (58,8%) y F2 (26,5%); 6 (10,7%) fueron tratados frente al VHC en pediatría con interferón y ribavirina sin éxito.
**Conclusiones:** A diciembre de 2014, un 12,6% de los pacientes de CoRISpe transferidos a Unidades de Adultos estaban coinfectados por VHC, encontrándose en el momento de la transición en estadio de fibrosis F2 el 26,5% y F3-F4 el 14,7%. Tanto los pacientes coinfectados como los monoinfectados por VIH presentaban buena situación inmunológica. Los pacientes coinfectados tenían un mejor control virológico y situación clínica, y recibían TAR en mayor porcentaje.

## Jueves, 3 de diciembre. Sala Auditorio (08:30-10:30 h)

### CO-11. EVOLUTION OF HIV-INFECTED INJECTING DRUG USERS IN SPAIN DURING 2004-2013: PERSISTENCE OF POOR ENGAGEMENT TO CARE AND CLINICAL OUTCOMES

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**Objective:** To compare late presentation (LP), delay in antiretroviral treatment (ART) initiation, response to ART, and progression to AIDS and death in patients who acquired HIV infection through use of injected drugs (IDU) compared to patients who acquired HIV by sexual transmission (ST: including men who have sex with men and heterosexuals).
**Methods:** Prospective multicenter cohort study of HIV-infected naïve subjects in Spain (CoRIS). LP, delayed ART initiation, and response to ART were assessed using multivariate logistic regression. Mortality and progression to AIDS were assessed by multivariate Cox regression and competing risks proportional hazards regression, respectively.
**Results:** A total of 9667 patients were included. The proportion of IDU progressively declined from 21.3% in 2004 to 3.8% in 2013. Compared to patients with ST, IDU had higher risk of LP (OR: 1.76; 95%CI: 1.41-2.18), delayed ART initiation (OR: 1.87; 95%CI: 1.44-2.42), and higher mortality (HR: 1.43; 95%CI: 1.03-2.01) and risk of progression to AIDS (SHR: 1.68; 95%CI: 1.29-2.18). Death was more frequently due to AIDS-defining causes in patients with ST (53.4%) than in IDU (36.6%; p = 0.002). The most frequent non-AIDS defining causes of death in IDU were liver-related in 23 (22.1%) and non-AIDS defining tumours in 13 (12.5%) patients. Virological response to ART was less frequent in IDU than in patients with ST, but only in patients without hepatitis C virus (HCV) infection. There were no significant differences in immunological response after adjusting by HCV.
**Conclusions:** The proportion of IDU has greatly declined over time in Spain, but they still remain an excluded group with poor engagement to care and worse outcomes. Compared with patients with sexual HIV transmission, IDU had a higher risk of delayed HIV diagnosis, delayed initiation of antiretroviral treatment, and progression to AIDS and death.

### CO-12. SLEEP DISTURBANCES IN A COHORT OF HIV-INFECTED CHILDREN AND ADOLESCENTS ON ANTIRETROVIRAL TREATMENT. NEUROCORISPES

C. García-Navarro[1], S. Jiménez de Ory[2], M.L. Navarro Gómez[2], J.T. Ramos Amador[3], M.J. Mellado[4], L. Prieto[5], P. Rojo Conejo[1], E. Núñez[6], M.I. González-Tomé[1] and Research Group CoRISpeS-Madrid Cohort

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**Background:** Sleep disorders have been reported in adults with HIV infection with a prevalence of at least 30%. Sleep quality (SQ) is very important in children and their daily functioning, although in HIV pediatric population scarce data are avalaible. Our objective was to assess SQ in our cohort and to determine the impact of antiretroviral therapy (ART).
**Methods:** HIV infected children and adolescents due to vertical transmission between 4 and 23 years old. They belonged to a national cohort (CoRISpeS) and were followed according to a standard protocol in several hospitals in Spain. Clinical characteristics, ART and adherence were registered. SQ was assessed through Pittsburgh Sleep Quality Index (PSQI), a questionnaire validated in Spanish population which assesses SQ and disturbances over a month. It scores for 7 components and one global score, distinguishing between good and poor sleepers. The most frequent regimen was 2NRTI+1NNRTI (46%), followed by 2NRTI+1PI (41%). For the analysis, we divided the sample into two groups according to the treatment they were receiving (NRTI+NNRTI vs NRTI+PI) in order to assess the influence of ART in sleep profile. Univariate and multivariate analysis (logistic regression) were performed.
**Results:** 59 patients were evaluated. Median age: 16 y (4, 23), age at start of ART: 0.62 y (0, 14), 66% females, 63% caucasian, AIDS-CDC category: 33.9% (13.6% encephalopathy). Median CD4 at baseline: 35% (1,59), CD4/CD8 1.0 (0.3, 28), nadir CD4: 15% (0.5, 45). Viral load < 50 cop/ml: 84.7%. Median time on HAART: 11.32 years (0.51, 17). Good adherence: 83%. No differences were found in clinical and immunovirological variables nor time of exposure to ART between both groups depending of their therapy (NRTI+NNRTI vs NRTI+PI). We found poor SQ in 24%, being the most frequent complaints: Sleep disturbances (76.3%), Sleep latency (59.3%), Subjective SQ (57.6%) and Daytime dysfunction (51.8%). Within the subgroups there were relationship between the use of NNRTI and Sleep latency (p = 0.021) and a trend in Habitual sleep efficiency (p = 0.066). Specifically, patients who took EFV presented longer sleep latency (p = 0.008) and Habitual sleep efficiency (p = 0.048). Age was also related to poorer SQ (p = .005). When we adjusted the analysis for age, relationship between the use of NNRTI and poorer SQ remained: Sleep latency (p = .027) and Efficiency (p = .088).
**Conclusions:** In our cohort sleep complaints are common. Mainly NNRTI and EFV seem to have an impact on SQ compared to PI regimens. We consider these results important in pediatric population due to the influence in daily functioning, school and cognitive performance.

## CO-13. VIRAL RESTRICTION BY NON-HUMAN TRIM5 ISOFORMS PROMOTES CD8+ T-RECOGNITION OF HIV-1 INFECTED CELLS

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**Background:** TRIM5 restricts Human Immunodeficiency Virus type-1 (HIV-1) in a species-specific manner by uncoating viral particles while activates early innate responses. Although the role of TRIM5 proteins in cellular immunity remains elusive, we hypothesized that it is possible through interactions with the incoming viral capsid (CA) and the cellular proteasome. Here we investigated whether the expression of non-human TRIM5 isoforms, Rhesus TRIM5a (RhT5) and TRIM-Cyclophilin A (TCyp), potent restrictors of HIV-1, could modulate CD8+ T-cell immune recognition of infected cells.
**Methods:** We transduced U937-B*2705 cells with lentiviral vectors encoding for RhT5 and TCyp genes or empty (EV) as control. To evaluate CD8+ T-cell mediated antiviral activity and killing in EV, RhT5 and TCyp cells infected with HIV-$1_{GFP}$, we measured the frequency of GFP+ cells and live cells by flow-cytometry in the absence or presence of HIV-1-specific CD8+ T cells. To test the specific role of TRIM5 to the activation of HIV-1-specific CD8+ T-cells, we quantified CD107a/MIP1B expression by intracellular cytokine staining in the presence of a non-immunosuppresive analogue of cyclosporin A, SmBz that blocks TRIM5 activity. In addition, we quantified IFN-γ production by Elispot in co-cultures with HIV-1 specific CD8+ T-cells recognizing Gag or Pol epitopes. Moreover, we measured viral uptake by intracellular $p24^{Gag}$ staining and quantified virus-proteasome contacts by immunofluorescence in EV, RhT5 and TCyp infected cells.
**Results:** Our data demonstrate the contribution of TRIM5 to CD8+ T-cell antiviral activity (TCyp vs EV; p = 0.003 and RhT5 vs EV; p = 0.003, respectively). Despite a potent HIV-1-specific CD8+ T-cell suppression in both TCyp- and RhT5-expressing cells, an increase in killing was only observed in HIV-1-infected RhT5 cells (RhT5 vs EV, p = 0.011). RhT5 and TCyp blocking experiments revealed a reduction of HIV-1-specific CD8+ T-cell activation (RhT5; p = 0.007 and TCyp; p = 0.03) that underscores the direct link between TRIM5 activity and CD8+ T-cell activation. Furthermore, the induction of CD8+ T-cell responses by HIV-1-infected cells was stronger for those expressing the RhT5 isoforms in the context of CD8+ T-cells recognizing the viral CA. The underlining mechanism involved the intracellular accumulation of the retroviral CA and the augment of virus-proteasome contacts in TRIM5 expressing cells.
**Conclusions:** In summary, we identified a novel role of non-human TRIM5 isoforms in cellular immunity. The RhT5 and TCyp non-human isoforms can couple viral restriction and CD8+ T-cell activation in HIV-1 infected cells. This mechanism of action should be exploited in order to develop novel therapeutic strategies to control HIV-1.

## CO-14. NANOLIPOSOMES TARGETING MYELOID CELLS TO DELIVER HIV-1 LATENCY REACTIVATORS TO LYMPHOID TISSUES

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**Background:** HIV-1 enters myeloid cells and infects bystander $CD4^+$ T cells via Siglec-1/CD169 recognition of viral membrane gangliosides. Siglec-1 is up-regulated on monocytes of infected patients, and we also detected this receptor on myeloid cells residing in lymphoid tissues. Here we aimed to engineer liposomal nanocarriers to mimic HIV-1 membranes and target Siglec-1 for efficient delivery of therapeutic cargo to lymphoid tissue.
**Methods:** Fluorescent PEGylated nanoliposomes were prepared with distinct sialyllactose-containing gangliosides (GM). Siglec-1+ primary myeloid cells were exposed to the same concentration of nanoliposomes. Capture was measured with fluorescence-activated cell sorting (FACS) and confocal microscopy. J-lat cells were used to assess reactivation activity measuring positive GFP cells by FACS. Statistical differences were assessed with a paired *t* test.
**Results:** Nanoliposomes prepared with increasing concentrations of GM led to an increased capture on myeloid cells ($P \leq 0.01$). Specificity for Siglec-1 was demonstrated by blocking capture with two monoclonal antibodies against Siglec-1 ($P \leq .0007$). Incorporation of PEG-lipids conferred a robust stability in up to 50% of serum, but

preserved Siglec-1 targeting ability. Fluorescent molecules of 10 kDa were efficiently encapsulated in the nanoliposomes and specifically delivered to the cytoplasm of Siglec-1+ cells only when they contained GM. Furthermore, nanoliposomes bearing romidepsin efficiently reactivated latently infected cells ($P \leq .038$) and were captured by Siglec-1+ myeloid cells in a GM dependent manner.
**Conclusions:** We have developed a nanocarrier system highly specific for Siglec-1+ myeloid cells located in peripheral blood and lymphoid tissues, a technology that could aid to deliver HIV-1 latency-reactivation molecules or candidate vaccines to key anatomical sanctuaries.
**Founding:** amfAR Mathilde Krim Fellowship 108676-55-RKRL.

## CO-15. TREATMENT OPTIONS AFTER VIROLOGICAL FAILURE OF FIRST-LINE TENOFOVIR-BASED REGIMENS IN SOUTH AFRICA

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**Background:** Tenofovir (TDF) is now a preferred first-line drug for antiretroviral treatment (ART) in resource-limited settings. Despite its high antiviral efficacy, failure to TDF-containing ART is associated with resistance to nucleoside and non-nucleoside reverse transcriptase inhibitors. This includes the selection of K65R mutation in about 50% of subjects according to Sanger sequencing-based assessments, which may underestimate the true burden of TDF resistance.
**Methods:** To generate an overall estimate of the prevalence of K65R mutation after TDF failure which also considered low-frequency K65R variants, we analysed the HIV-1 pol sequence of plasma samples of subjects developing virological failure to first-line ART including TDF in a prospective South African cohort. All samples were first evaluated with Sanger sequencing. Those with no K65R detection were further analysed with deep sequencing in a MiSeq platform (Illumina). A 1% threshold level was chosen for detection of minority variants. We also analysed the detection of other relevant resistance NNRTI and NRTI mutations, defined according to the IAS-USA 2014 update, and used the HIVdb program to predict drug susceptibility.
**Results:** Eighty-eight subjects who developed VF on TDF-containing ART were sequenced by Sanger. Amplification failed in 9 samples (10.2%) leaving 79 evaluable subjects. Sanger sequencing detected K65R mutation in 47/79 samples (59.5%). Deep sequencing was attempted in the remaining 32 samples. However, 5/32 samples had been used completely and could not be further evaluated. Mutation K65R was found in 8/27 samples by MiSeq (30.0%) at frequencies in the virus population ranging 1.3% to 32.5%. Considering Sanger and deep sequencing results together and assuming that none of the 5 subjects not evaluable by MiSeq had the K65R mutation, a conservative estimate of the overall prevalence of K65R mutation was 70.0%. Overall, deep sequencing detected IAS-USA mutations missed by Sanger in 22/27 subjects (81.4%) at frequencies ranging 1.1% to 35.7% in the virus population. Such additional mutations changed predicted drug susceptibility in 15/27 subjects (55.5%). Considering MiSeq data, 21/27 (77.7%), 25/27 (92.6%), 13/27 (48.1%) and 15/27 (55.5%) were resistant to 3TC/FTC, NVP/EFV, ETR and RPV, respectively, whereas only 3 subjects (11.1%) had intermediate resistance to AZT.
**Conclusions:** Most subjects developing virological failure to TDF-containing regimens are resistant to TDF, as well as to FTC/3TC, EFV, NVP, ETR or RPV. Availability of highly sensitive but affordable genotyping tools in resource-limited settings would assist in identifying which of these drugs could be used combined with AZT and ritonavir-boosted PI for second-line ART.

## CO-16. DETECTION OF ANAL HPV INFECTION BY TWO TECHNIQUES IN HIV+ MSM INDIVIDUALS AND CORRELATION WITH PATHOLOGIC FINDINGS IN CYTOLOGY AND BIOPSY

I. Bravo[1], E. Ferrer[2], M.S. Di Yacovo[2], I. Catalá[1], N. Baixeras[1], S. Tous[1], L. Trentis[2], M. Torres[1], B. García-Vidal[2], J. Curto[2], F. Gili[2], S. San José[2] and D. Podzamczer[2]

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**Objective:** To detect anal HPV infection by two techniques in HIV+ MSM individuals and to correlate with pathologic findings in cytology and biopsy.
**Methods:** All consecutive HIV+ MSM patients followed between January 2014 and January 2015 in our anal cancer prevention program (n = 159) were explored to detect anal HPV infection. Anal swabs provided samples for cytology and for HPV detection by High-Risk Hybrid-Capture2 (HC2) and by Linear Array HPV Genotyping test (LA). A high resolution anoscopy with biopsy was performed in patients with abnormal cytology.
**Results:** Median age was 44 (range: 22-72) years, CD4 T cell count 714(224-1683) cells/uL; CD4 nadir 264 (3-832); 98% were on Anti-retroviral Treatment (ART); 93% displayed undetectable HIV viral load; 20% had AIDS; and 25% had previous diagnosis of anal warts. Infection by any HPV was detected in 90.6% of cases by LA. Infection by oncogenic HPVs was detected in 53.5% by HC2 and in 77.4% by LA (Table). 81.9% of the infections contained multiple HPVs (median = 3), with 56% patients being simultaneously infected by between three and ten HPVs. The most frequent type was HPV16 (30.6%). 156 cytologies rendered valid results: 68% were normal; 18% ASCUS; 14% LSIL; 7% HSIL; and 2.5% ASCH. Proportion of HPV infection was significantly lower in patients with normal cytology using both techniques: 86.8% vs 100% for LA (p = 0.041) and 39.6% vs 87.9% for HC2 (p < 0.001). Biopsies were performed in 27 (17%) patients: 22% were normal 22%; 56% AIN I/II/III; and 22% other diagnoses. Normal findings were associated with lower incidence of oncogenic HPV by HC2 (p = 0.003) but not by LA (p = 0.5).
**Conclusions:** LA seems more sensitive and HC2 more specific in the detection of anal HPV infection. The vast majority of our study population presented simultaneous infections by multiple HPVs. Proportion of HPV infection was significantly lower in patients with normal cytology/biopsy.

**Table CO-16.** Detection of anal HPV infection by LA and HC2 techniques

| HPV Detection | | Cytology | | | | Total | |
|---|---|---|---|---|---|---|---|
| | | Normal | | LSIL/HSIL | | | |
| | | N | % | N | % | N | % |
| LA | Negative | 14 | 13.2 | 0 | 0.0 | 14 | 10.1 |
| | Positive | 92 | 86.8 | 33 | 100.0 | 125 | 89.9 |
| Total | | 106 | 100.0 | 33 | 100.0 | 139 | 100.0 |
| HPV Detection | | Cytology | | | | Total | |
| | | Normal | | LSIL/HSIL | | | |
| | | N | % | N | % | N | % |
| HC2 | Negative | 64 | 60.4 | 4 | 12.1 | 68 | 48.9 |
| | Positive | 42 | 39.6 | 29 | 87.9 | 71 | 51.1 |
| Total | | 106 | 100.0 | 33 | 100.0 | 139 | 100.0 |

## CO-17. EFFICACY AND SAFETY OF SIMEPREVIR, DACLATASVIR AND RIBAVIRIN IN PATIENTS WITH RECURRENT HEPATITIS C VIRUS GENOTYPE 1B INFECTION AFTER ORTHOTOPIC LIVER TRANSPLANTATION (OLT): RESULTS FROM THE PHASE II SATURN STUDY

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**Target/Background:** Post-transplant recurrence of hepatitis C virus (HCV) infection is universal in patients with detectable HCV RNA at the time of orthotopic liver transplantation (OLT). SATURN is an ongoing, open-label, Phase II study (NCT01938625) investigating the safety and efficacy of simeprevir (SMV; a NS3/4A protease inhibitor), daclatasvir (DCV; a NS5A replication complex inhibitor) and ribavirin (RBV) for 24 weeks in patients with recurrent HCV genotype (GT)1b infection after OLT.
**Methods:** GT1b-infected, treatment-naïve or treatment-experienced post-OLT patients on stable immunosuppressive therapy were included. One GT1a-infected patient was included erroneously. Part 1 (P1) included patients with METAVIR score F1–F2 receiving cyclosporine (CsA; n = 10) or tacrolimus (TAC; n = 11). Part 2 (P2) included F1–F4 patients receiving TAC (n = 14). Patients received SMV 150mg once daily (QD)+DCV 60 mg QD+RBV 0.8–1.2 g/day for 24 weeks. The primary efficacy endpoint was sustained virologic response 12 weeks after end of treatment (SVR12). Safety outcomes were assessed. All patients had reached the SVR12 time point or discontinued earlier.
**Results:** In total, 35 patients were included (CsA/TAC, 29%/71%; male, 63%; median age, 62 years; treatment-naïve, 63%; *IL28B* CC/CT/TT, 26%/51%/23%; median time since OLT, 4.2 years; median baseline HCV RNA, 6.9 $\log_{10}$ IU/mL; METAVIR F1/F2/F3/F4, 37%/40%/9%/14%). In P1, CsA patients had ~3-fold higher SMV plasma concentrations than TAC patients, leading to SMV dose adjustments (from 150 mg QD to 150 mg every other day in 8/10 patients who had SMV trough concentrations > 7300 ng/mL) and the exclusion of CsA patients from P2. Overall, 32/35 (91%) patients achieved SVR12 (CsA: 100%/TAC: 88%). All 3 (9%) patients not achieving SVR12 were receiving TAC and had viral breakthrough between Weeks 12–20 of treatment. One of the 3 patients with viral breakthrough had GT1a infection; the remaining 2 patients were GT1b-infected, with *IL28B* CT and NS5A emerging mutations at time of failure (1 treatment-naïve with METAVIR score F2 and 1 treatment-experienced with METAVIR score F4). Adverse events (AEs) were observed in 35 (100%) patients (Grade 1/2: 71%/Grade 3/4: 29%). Most frequently reported AEs (> 15% patients) were anaemia (54%), asthenia (34%) and pruritus (17%). Eight (23%) patients had serious AEs (CsA: 40%/TAC: 16%) and 1 (3%) patient discontinued all study medications due to an AE (hyperbilirubinaemia). Grade 3/4 abnormalities for the laboratory parameters hyperbilirubinaemia and decreased haemoglobin were reported in 34% (CsA: 40%/TAC: 32%) and 6% of patients, respectively.
**Conclusions:** SMV+DCV+RBV led to an SVR12 rate of 94% (32/34) in GT1b-infected patients and was generally well tolerated in post-OLT patients on immunosuppressive therapy.
**Funding:** Janssen.

## CO-18. EXPERIENCIA EN EL TRATAMIENTO DE VHC CON LOS NUEVOS ANTIVIRALES DE ACCIÓN DIRECTA (AAD) EN PACIENTES COINFECTADOS CIRRÓTICOS EN EL PAÍS VASCO

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**Objetivo:** Analizar la respuesta al tratamiento en pacientes tratados con AAD en 4 hospitales universitarios de la comunidad autónoma del País Vasco: H. Araba, H. Basurto, H. Donostia y H. Cruces.
**Material y métodos:** Se ha realizado un estudio descriptivo retrospectivo de los casos de pacientes VHC- VIH que iniciaron tratamiento en el periodo 2/12/2014 a 27/05/15 y que han finalizado el tratamiento con AAD en los 4 centros hospitalarios. Se han revisado las bases de datos de cada hospital para analizar los diferentes esquemas de tratamiento utilizados, la respuesta virológica obtenida, el grado de fibrosis mediante FibroScan® y la tolerabilidad del tratamiento.
**Resultados:** Han finalizado el tratamiento 89 pacientes, 68,47% varones, con mediana de edad de 51. La mediana del grado de fibrosis fue 31 kPa y el 96.55% se encontraban en fase de cirrosis (F4). El 62.9% presentaban genotipo 1, el 1.1% genotipo 2, el 16% genotipo 3 y el 20% genotipo 4. Disponemos de datos de respuesta virológica a las 4 semanas de finalización del tratamiento en 66 pacientes; el resto se encuentran pendientes de valoración de respuesta, se han perdido el seguimiento o han fallecido en ese periodo. El 83.92% de los pacientes ha recibido tratamiento durante 12 semanas y el 16.08% durante 24 semanas. La tasa global de respuesta viral a las 4 semanas post-finalización ha sido del 86,36% (57 pacientes). En los pacientes que han completado el tratamiento los esquemas empleados y la respuesta a las 4 semanas de tratamiento fueron: sofosbuvir + simeprevir ± ribavirina – 49 pacientes. RV en 83,67% (41 pacientes); sofosbuvir + peg-interferón + ribavirina – 9 pacientes. RV en 88,88% (8 pacientes); paritaprevir + ombitasvir + dasabuvir – 1 paciente. RV en 100%; daclatasvir + sofosbuvir + ribavirina – 6 pacientes. RV en 83,33% (5 pacientes); simeprevir + daclatasvir + ribavirina – 1 paciente. RV en 0%. Los pacientes tratados han presentado buena tolerancia al tratamiento. Se ha suspendido el tratamiento por toxicidad en 1 paciente y 1 paciente lo abandonó. Únicamente un 16,6% precisó descenso de dosis de RBV.
**Conclusiones:** Se ha obtenido una alta tasa de respuesta viral sostenida a las 4 semanas post-finalización en nuestra serie de pacientes cirróticos. La tolerabilidad del tratamiento ha sido muy buena con muy pocas retiradas por toxicidad. Las nuevas pautas de tratamiento representan un avance terapéutico significativo en el tratamiento de los pacientes coinfectados.

## CO-19. DETERMINACIÓN DEL VIRUS DEL PAPILOMA HUMANO EN TRACTO GENITAL INFERIOR COMO MÉTODO DE CRIBADO DE PATOLOGÍA ANAL EN MUJERES SEROPOSITIVAS

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**Antecedentes:** Las pacientes infectadas por el virus de la inmunodeficiencia humana (VIH) presentan mayor incidencia de infección por el virus del papiloma humano (VPH) en el tracto genital inferior (TGI), así como de lesiones cito-histológicas derivadas de dichas infecciones. La mayor persistencia de la infección VPH y la interacción

sinérgica entre VIH-VPH, asociadas al grado de inmunosupresión, conllevan una mayor probabilidad de progresión de lesiones intraepiteliales a cáncer. La incidencia de cáncer anal es de 70/100.000 pacientes VIH. El objetivo principal fue determinar la relación entre el VPH en TGI y las displasias anales (DA). Como objetivo secundario; demostrar la importancia del cribado de las DA en estas pacientes.
**Material y métodos:** Estudio observacional de corte transversal prospectivo desde octubre de 2012 hasta diciembre de 2014. Se seleccionaron las pacientes seropositivas remitidas a la consulta de Patología Cervical (n = 76) para el cribado de patología cervical y anal. Variables a estudio: epidemiológicas, evolución de la infección VIH, resultados anatomopatológicos y microbiológicos de las muestras cervicales y anales. Estudio estadístico con el paquete SPSS19. p < 0,05 determinó el nivel de significación estadística.
**Resultados:** 76 mujeres VIH. Edad media 44 años (22-62). La edad media de inicio de las relaciones sexuales fue a los 17 años (13-33). Más de la mitad no empleaban método anticonceptivo. La carga viral basal media fue de 4517 copias/ml pero, más del 80% presentaban carga viral indetectable en el momento del cribado. Los niveles de CD4 se situaron entre 28 y 1518/mmc. El 25,7% de las citologías anales resultaron alteradas. Y más de la mitad de las muestras presentaron un VPH de alto riesgo (AR) (63,2%). En las muestras cervicales, se obtuvo un 35,5% de citologías positivas y un 67,1% de VPH-AR. La relación entre la patología anal y el VPH anal fue estadísticamente significativa (p = 0,00). Así, el 92,3% de las citologías anales negativas presentaron VPH-AR oncogénico negativo. O lo que es lo mismo, el 85,7% de los VPH anales presentaban una citología anal negativa. Al estudiar la relación entre las citologías anales alteradas y la presencia de VPH anal y/o cervical esta también alcanzó significación estadística. De tal modo que prácticamente el 100% (94,1%) de las citologías anales alteradas presentaban un VPH-AR en el TGI.
**Conclusiones:** La presencia del VPH en el TGI presentó una relación estadísticamente significativa con las displasias anales. La determinación de VPH en TGI femenino debería valorarse como prueba de cribado de la patología anal en mujeres VIH.

## CO-20. ESTUDIO PROSPECTIVO PARA LA DETECCIÓN PRECOZ DE CARCINOMA PULMONAR EN PACIENTES CON INFECCIÓN POR VIH: RESULTADOS PRELIMINARES

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**Objetivo:** El carcinoma pulmonar (CP) es la tercera neoplasia en frecuencia en la población con VIH, pero hasta fechas recientes no ha existido un método para diagnosticarlo en estadios precoces. Se describen los resultados preliminares de un protocolo cuyo objetivo principal es evaluar la rentabilidad de la realización de un TAC torácico de baja radiación sin administración de contraste (TC) en un grupo de pacientes con alto riesgo de desarrollar CP.
**Pacientes y métodos:** Los criterios de inclusión son: edad > 45 años, fumador de > 20 paquetes/año y nadir CD4+ < 200 mm$^3$. Tras firmar el consentimiento informado se realiza un TC que se repetirá anualmente durante los 4 años siguientes. Se estableció el hallazgo de un nódulo > 8 mm como límite para iniciar exploraciones complementarias que descarten CP.
**Resultados:** Hasta el momento se ha realizado el TC inicial en 36 pacientes cuyas características aparecen reflejadas en la tabla adjunta. En 16 pacientes (44,4%) se objetivaron nódulos < 4 mm, en 4 (11,1%) entre 4-8 mm y solo en uno se detectó un nódulo > 8 mm que obligó a la realización de fibrobroncoscopia sin confirmarse la presencia de CP. Existieron otros hallazgos que condicionaron exploraciones complementarias: un ecocardiograma en 5 pacientes por presentar datos de hipertensión pulmonar (13,9%) y un angioTC en 3 por el hallazgo de un aneurisma de aorta (8,3%). Además, se encontraron lesiones residuales de TBC en 22 pacientes (61,1%), datos de EPOC en 11 (30,6%) y calcificación de arterias coronarias y/o válvulas cardiacas en 15 (41,7%).
**Conclusiones:** Los resultados preliminares demuestran la existencia de múltiples patologías torácicas en este subgrupo de pacientes y justifican continuar el estudio para poder establecer su evolución y la naturaleza y evolución de los nódulos encontrados.

**Tabla CO-20**

| | N = 36 | % |
|---|---|---|
| Varones | 31 | 86,1 |
| Edad (mediana años, IQR) | 57, IQR 56-61 | |
| Raza caucásica | 34 | 94,4 |
| Años de infección (mediana, IQR) | 24,5, IQR 19-26,7 | |
| Conducta de riesgo | | |
| Sexual | 22 | 61,1 |
| Parenteral | 12 | 33,3 |
| Sexual+Parenteral | 1 | 2,8 |
| Desconocido | 1 | 2,8 |
| TAR basado en: | | |
| IP | 4 | 11,1 |
| No análogo | 12 | 33,3 |
| Inhibidor integrasa | 5 | 13,9 |
| Biterapia | 9 | 25 |
| Monoterapia | 3 | 8,3 |
| Otros | 3 | 8,3 |
| Hepatitis crónica VHB | 2 | 5,6 |
| Hepatitis crónica VHC activa | 6 | 17,6 |
| Estadio CDC | | |
| A3 | 9 | 25 |
| B3 | 12 | 33,3 |
| C3 | 15 | 41,7 |
| Carga viral indetectable | 36 | 100 |
| Mediana linfocitos CD4+ al realizar TC (mediana, IQR) | 566, IQR 346-864,7 | |
| Mediana nadir de linfocitos CD4+ (mediana, IQR) | 97,5, IQR 97,5-168,7 | |