#1

Hepatic infusion of autologous bone marrow promotes immune reconstitution in a patient suffering from HIV Kaposi's sarcoma

Baochi L[1]
[1]*Departmento o f Surgery, Shanghai Public Health Clinical Center Affiliated to Fudan University*

Chemotherapy may aggravate the immune damage of AIDS with malignant tumors, but chemotherapy is a necessary treatment.One patient with AIDS complicated with kaposi's sarcoma developed severe immune damage and perianal infection after a course of chemotherapy. Sigmoid colostomy and intravenous catheterization were performed.Before the second chemotherapy, autologous bone marrow was collected for preservation, and 5 days after the end of chemotherapy, the bone marrow was transferred back to the port by buried infusion.The bone marrow was preserved before each chemotherapy and the preserved bone marrow was restored after chemotherapy.After 6 times of chemotherapy, CD4+ T cells increased and infection around anus healed.It is suggested that the preservation of autologous bone marrow before chemotherapy and the transfusion of preserved autologous bone marrow via the sigmoid vein to the portal vein after chemotherapy can promote the immune reconstruction after chemotherapy.
Kaposi's sarcoma, also known as multiple idiopathic sarcoma, is a multicentric vascular tumor. It is rather common type tumor in AIDS patients, but rare in the general population. When Kaposi's sarcoma occurs in conjunction with AIDS, treatment is often difficult. Chemotherapy is currently the treatment of choice, however, its damage to the already weakened immune system of AIDS patients can lead to infectious complications and even mortality. In a Kaposi's sarcoma AIDS patient suffering from severe herpes infection around the anus, we preserved autologous bone marrow prior chemotherapy. Upon completion of chemotherapy, we infused the preserved autologous one marrow via the hepatic portal vein. We found that the strategy is highly efficacious in rebuilding the immune system. The results are reported herein.

#2

Curative effect of autologous bone marrow cell transplantation in HIV-infected patients with decompensated liver cirrhosis

Baochi L[1]
[1]*Department of Surgery, Shanghai Public Health Clinical Center Affiliated to Fudan University*

Objective: This study aimed to investigate the effect of splenectomy combined with autologous bone marrow cell (BMC) transplantation through the portal vein in human immunodeficiency virus (HIV)-infected patients with decompensated liver cirrhosis (DLC).

Methods: Twenty one patients diagnosed with DLC and HIV infection underwent antiretroviral therapy and hepatoprotective therapy. The routine therapy group included 7 patients who underwent only routine therapy, and the combination therapy group included 14 patients who underwent splenectomy among them 12 patients were given autologous BMC transplantation through the portal vein. A long-term follow-up study was performed using flow cytometry and biochemical markers to detect the cellular immunity markers.

Results: In the routine therapy group, six patients died of gastrointestinal bleeding and liver failure in two years and one died of liver failure in the third year. In the combination therapy group, two patients died of postoperative bleeding and liver failure in three days after operation. Moreover, in the combination therapy group, the liver function score was significantly higher, the levels of albumin were significantly increased, and the total bilirubin and prothrombin time were significantly reduced or shortened compared with the routine therapy group. The white blood cell count, hemoglobin, platelet count, and CD4+ and CD8+ levels were significantly higher in the combination therapy group at different time points compared with the routine therapy group.

Conclusions: The effect of splenectomy combined with autologous BMC transplantation through the portal vein in HIV-infected patients with DLC was obvious. Also, the combination therapy promoted the functional reconstruction of liver synthesis and secretion and was closely related to the reconstruction of cellular immune function of the body.

#3

A Model to Predict In-Hospital Mortality in HIV/AIDS Patients with Pneumocystis Pneumonia in China: The Clinical Practice in Real World

Wu L[1,2], Xiao J[1,2], Zhao H[1,2]
[1]Clinical and Research Center of Infectious Diseases, Beijing Ditan Hospital, Capital Medical University, [2]The National Clinical Key Department of Infectious Diseases, Beijing Ditan Hospital, Capital Medical University

We aimed to develop and validate a predictive model to evaluate in-hospital mortality risk in HIV/AIDS patients with PCP in China. 1001 HIV/AIDS patients with PCP admitted in the Beijing Ditan hospital from August 2009 to January 2018 were included in this study. Multivariate Cox proportional hazard model was used to identify independent risk factors of death, and a predictive model was devised based on risk factors. The overall in-hospital mortality was 17.3%. The patients were randomly assigned into derivation cohort (801cases) and validation cohort (200 cases) in 8:2 ratio, respectively, in which in derivation cohort we found that 7 predictors, including LDH >350U/L, HR>130 times/min, room air PaO2 <70mmHg, later admission to ICU, Anemia (HGB≤90g/L), CD4<50cells/ul, and development of a pneumothorax, were associated with poor prognosis in HIV/AIDS patients with PCP and were included in the predictive model. The model had excellent discrimination with AUC of 0.904 and 0.921 in derivation and validation cohort, respectively.The predicted scores were divided into two groups to assess the in-hospital mortality risk: low-risk group (0-11 points with mortality with 2.15-12.77%) and high-risk group (12-21 points with mortality with 38.78%-81.63%). The cumulative mortality rate also indicated significant difference between two groups with Kaplan-Meier curve ($p<0.001$). A predictive model to evaluate mortality in HIV/AIDS patients with PCP was constructed based on routine laboratory and clinical parameters, which may be a simple tool for physicians to assess the prognosis in HIV/AIDS patients with PCP in China.

#4

Critical amino acid residues and potential N-linked glycosylation sites contribute to CRF01_AE pathogenesis in Northeast China

Wang F[1]

[1]The thrid people's hospital of Shenzhen / 深圳市第三人民医院, [2] 哈尔滨医科大学

Background: The wide and fast transmission of circulating recombinant form (CRF) 01_AE strain played a critical role in diversity and complexity of HIV-1 infection in China. Nowadays, CRF01_AE strains have formed several stable transmission clusters in different regions of China, and one cluster was epidemic in Northeast China (Heilongjiang, Jilin and Liaoning provinces). This CRF01_AE cluster dominated the subtype in this region, and showed a tendency for a longer growth period compared to the other CRF01_AE clusters in China. Therefore, understanding the factors associated with CRF01_AE transmission and pathogenesis is urgently required for the control and prevention of this subtype infection in China.

Material & Methods: The genotypes of newly identified strains were determined by phylogenetic analyses using Mega 6.06. Coreceptor usage was predicted by Geno2Pheno algorithm. Potential N-linked glycosylation site (PNGS) number was calculated using the online N-glycosite software. The properties of amino acid sequences were analyzed by the online ProtParam tool. Compared analysis was made between CRF01_AE and non-CRF01_AE samples to understand the pathogenicity features of CRF01_AE. Further analyses between CRF01_AE samples with high or low CD4 cell counts and between samples with different coreceptor usages were done to explore the possible factors correlating to the pathogenesis of CRF01_AE viruses.

Results: CRF01_AE become the main HIV-1 genotype in Jilin province of the Northeast China since 2010. Compared with non-CRF01_AE group, the CRF01_AE group showed a higher proportion of samples with CD4 count less than 200 cells/μL. Shorter amino acid length, fewer PNGSs and the presence of a basic motif R/KNXT or NR/KT in V4 correlated to a lower CD4 count, and existence or co-existence of Thr12, Arg13, Val21 and Lys33, presence of more than 4 of net charges and lack of the PNGS within V3 favored to the X4/R5X4 coreceptor usage of CRF01_AE viruses.
Conclusion: CRF01_AE has dominated HIV-1 genotype in Northeast China. Infection with CRF01_AE exhibited a fast disease progression, which may be associated with specific amino acid residues and PNGSs in V3 and V4 regions as well as amino acid length of V4 region.

5

Study on the effect of PERMA mental model on drug adherence in HIV/AIDS outpatients

Wang WF[1], Lin Y[1], Zeng HY[1], Cheng QH[1], LV JN[1]
[1]*Beihai people's hospital*

Background and Aim: Improving the medication compliance of outpatient HIV/AIDS patients is one of the important means to achieve the "Three 90%" goal proposed by the United Nations program. In particular, the research on strengthening psychological support to improve medication compliance has become a hot issue at present.The aim of the present study was to investigate the effect of the PERMA psychological model on emotions of HIV/AIDS patients， to provide a theoretical basis for improving drug adherence of HIV/AIDS patients.

Methods: A total of 75 HIV/AIDS patients were randomly selected from the VCT clinic of Beihai Beihai People's Hospital from January to December 2017 . They were randomly divided into intervention group (n = 38) and control group (n = 37). All subjects were treated with HAART therapy, the control group was given five consecutive interviews with health education, and five consecutive positive psychological interviews were conducted on the intervention group around the PERMA psychological model. The patients in the two groups were assessed by PANAS, IWB and WHOOL-HIV-BREF before intervention, after intervention and one month after intervention. Two groups of patients were investigated by CPCRA and evaluated the difference of drug adherence. The average CD4+T lymphocyte count was calculated by flow cytometry in both groups to evaluate the changes of immunological indicators at 1 year after intervention.

Results: 1. There were no statistically significant differences in scores of quality of life, positive rate and well-being index between the two groups before intervention. 2. In addition to the environmental field of quality of life, the main effects of intervention in other areas of quality of life, positive rate and well-being were statistically significant ($P < 0.05$); The time main effect of quality of life, positive rate and well-being index score were also statistically different between the two groups ($P < 0.05$). 3. The number of times of missing and non-compliance in the intervention group was less than that in the control group, and the adherence (94.23%) was higher than that in the control group (82.45%) ($P < 0.05$). 4. After 12 months of HAART treatment, the average CD4+T lymphocyte count in the intervention group was 266.8 /ul, significantly higher than 212.5 /ul in the control group ($P < 0.05$).

Conclusions: The PERMA psychological model can eliminate the negative emotions, improve the quality of life and the life well-being of HIV/AIDS outpatients. It play a positive role in improving drug adherence and HAART efficacy.

#6

Baseline analysis of a long-term off-treatment follow-up study to assess clinical outcomes in chronic Hepatitis C patients in China previously treated with daclatasvir-based regimens

Hou J[1], Xie Q[2], Lu W[3], Zhang M[4], Yin C[5], Yang Y[6], Jia Z[7], Rao H[8], Li J[9], Tan Y[10], Tang H[11], Ning Q[12], Wang M[13], Wu S[14], Xie W[15], Wang G[16], Jin Q[17], Chen X[18], Du Q[19], Sun Y[20]

[1]Nanfang Hospital, [2]Ruijin Hospital, Shanghai Jiaotong University School of Medicine, [3]The Second People's Hospital of Tianjin, [4]The Six People's Hospital of Shenyang, [5]No.8 People's Hospital of Guangzhou City, [6]The Second Hospital of Nanjing, [7]Tangdu Hospital, [8]Peking University People's Hospital, [9]The First Affiliated Hospital of Nanjing Medical University, [10]The Third People's Hospital of Zhenjiang, [11]West China Hospital of Sichuan University, [12]Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, [13]PLA General Hospital of Eastern Theater Command(PLA 81st Hospital), [14]Shanghai Public Health Clinical Centre, [15]Beijing Ditan Hospital Capital Medical University, [16]Peking University First Hospital, [17]The First Bethune Hospital of Jilin University, [18]Beijing Youan Hospital of Capital Medical University, [19]Fountain Medical Development LTD., [20]BMS

Background: Hepatitis C virus (HCV) infection represents a considerable healthcare burden in China, with an estimated 10 million cases of infection. Direct-acting antiviral agents (DAA), including daclatasvir (DCV) plus asunaprevir (ASV), have demonstrated improved efficacy and safety profiles. The DCV-based regimen was the first to be approved; 9 DAA regimens have since been approved in China. Long-term data on disease outcomes and the durability of virologic response are limited. This follow-up study therefore aims to assess the long-term clinical outcomes in Chinese patients treated with approved DCV-based regimens for chronic HCV infection; baseline patient data are presented.

Methods: A multicentre, non-interventional, prospective cohort study across 20 sites in China. Target enrolment is 1,000 patients from two Phase III clinical trials (NCT01995266 and NCT02496078) and eligible real-world patients. Inclusion criteria are prior, on-label treatment with a DCV-based regimen for ≥8 weeks and age ≥18 years at initiation of DCV-based treatment. Cut-off for enrolment is <12 months from end of DCV-based therapy or <6 months from protocol availability at the Phase III centre. Patients are to be followed for five years, with assessments performed according to routine, local clinical practice. The primary endpoint is assessment of hepatic disease progression; secondary endpoints include durability of virologic response, change in liver stiffness, evolution of HCV sequence variants over time in virologic failures, and retreatment patterns in patients that failed DCV-based therapy.

Results: Between 30 October 2017 and 15 December 2018, 143 patients were enrolled in the study. Most patients (n=130, 90.9%) had received DCV+ASV therapy as 106 patients (74.1%) were enrolled from the two Phase III clinical trials of DCV+ASV; eight patients had been treated with DCV + sofosbuvir. At baseline, prior to commencing DCV-based therapy, 72.0% (n=103) of patients were female, median age was 55 years (range 24–78), 108 (78.8%) were non-cirrhotic and 29 (21.2%) had diagnosed cirrhosis (28 compensated cirrhosis, one decompensated cirrhosis). Mean (standard deviation [SD]) liver stiffness measurements were 11.3 (9.0) kPa in the total population and 23.5 (10.0) kPa in patients with cirrhotic liver disease. Most participants (97.1%) had HCV GT1b infection, with a viral load ≥800,000 IU/mL detected in 113 patients (83.7%). In the subset of patients (n=9) who had both pre- and post-treatment liver stiffness measurements, mean (SD) decrease in liver stiffness after treatment was 3.5 (10.2) kPa. Among patients with efficacy results, 86.5% (109/126) had a sustained virologic response at 12 or 24 weeks (SVR12/24).

Conclusions: Most patients enrolled in the study had received DCV+ASV for the treatment of HCV GT1b infection and were non-cirrhotic. Liver stiffness regression in evaluable patients and high rates of SVR12/24 were achieved following DCV-based therapy. This follow-up study will evaluate the long-term clinical benefits of DCV-containing antiviral regimens over a period of five years post-treatment.

#7

A Phase 3b, Open-Label, Pilot Study to Evaluate Switching to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) in Virologically-Suppressed HIV-1 Infected Adult Subjects Harboring the NRTI Resistance Mutation M184V and/or M184I (GS-US-292-1824)

Perez-Valero I[1], Llibre JM[2], Lazzarin A[3],Di Perri G[4], Pulido F[5], Molina JM[6], McNicholl IR[7], Lorgeoux RP[8], Margot N[7], Shao Y[7], Piontkowsky D[7], Das M[7], Zheng T[9], Haubrich R[7]

[1] Unidad VIH - Hospital Universitario La Paz, Madrid, Spain.[2] Fundación Lucha contra el SIDA, Barcelona, Spain,[3] Fondazione IRCCS San Raffaele del Monte Tabor, Milan, Italy,[4] Dipartimento di Malattie Infettive e Tropicali, Turin, Italy,[5] Unidad VIH, Hospital Universitario 12 de Octubre, imas12, UCM, Madrid, Spain,[6] Department of Infectious Diseases, Saint-Louis Hospital and University of Paris, Paris, France,[7] Gilead Sciences, Foster City, CA, USA,[8] Gilead Sciences, Montreal, Canada,[9] Gilead Sciences, Ltd, Shanghai,China

Background: Treatment with once-daily E/C/F/TAF in HIV-1-infected therapy-naïve patients was shown to be effective and safe through 144 weeks in two randomized, double-blinded trials, which excluded participants whose HIV-1 harbored the M184V and/or M184I mutation.

Methods: This ongoing, prospective open-label, single arm, multicenter, 48-week trial is evaluating the efficacy and safety of switching suppressed participants to E/C/F/TAF from a stable regimen (≥6 months) of a third agent plus either F/tenofovir disoproxil fumarate or abacavir/lamivudine. Participants had a historical genotype report showing M184V and/or M184I and no evidence of previous virologic failure (VF) or resistance to boosted PIs or INSTIs. At screening, HIV-1 RNA <50 c/mL was required as well as absence of additional NRTI or PI resistance mutations based on sequencing of integrated HIV DNA (GenoSure Archive, Monogram Biosciences). The primary objective is to evaluate the efficacy of switching to E/C/F/TAF in maintaining HIV-1 RNA <50 c/mL at Week 12 using pure virologic response (PVR). Participants with discontinuation or missing values were considered responders if they *never* had HIV-1 RNA ≥50 c/mL at 2 consecutive visits and the last HIV-1 RNA was <50 c/mL. This report presents the Week 24 data.

Results: Thirty-seven participants were enrolled and switched to E/C/F/TAF. Mean age was 50 years (range 22-76), 73% White, 19% Black, 22% women, median CD4 count 724 cells/µL and 100% HIV RNA <50 c/mL at baseline. Through Week 24, all 37 participants (100%) had HIV-1 RNA <50 c/mL based on PVR. Three participants who discontinued prior to Week 24 with last recorded HIV-1 RNA <50 c/mL were not considered VF. Four serious adverse events occurred (none were study drug-related): 1 each of squamous cell carcinoma, acute kidney injury (with poorly controlled hypertension and diabetes), transient proteinuria (resolved on study drug) and pulmonary embolism. Twenty-two percent (8/37) of participants experienced a study drug-related AE (grade 1 or 2); one participant discontinued due to grade 2 muscle spasms.

Conclusions: E/C/F/TAF offers an effective, well tolerated switch option for patients with pre-existing M184V and/or M184I mutations. These data on continued virologic suppression despite resistance are encouraging though longer term data are needed.

#8

Phase 3b, Randomized, Open-Label Study to Evaluate Switching from a Tenofovir Disoproxil Fumarate (TDF) Containing Regimen to Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) in Virologically-Suppressed, HIV-1 Infected Participants Aged ≥60 Years

Maggiolo F, Rizzardini G, Pulido F, Mateo Garcia GM, Molina JM, Ong E, Shao Y, Corales R, McNicholl I, Piontkowsky D, Das M, Hygieia Liu, Haubrich R

Background: With many people living with HIV who are now >50 years old, the long-term safety in addition to efficacy of HIV treatment continues to be paramount. TAF is a tenofovir prodrug associated with 90% lower tenofovir plasma levels than TDF resulting in less renal and bone toxicity. We evaluated bone mineral density (BMD) changes after switching participants 60 years and older from a TDF to a TAF-containing regimen.

Material and Methods: Virologically suppressed (HIV-1 RNA <50 copies/mL) participants, age ≥60 years on a TDF-containing regimen were randomized (2:1) to open-label E/C/F/TAF or continued TDF-based regimen (TDF). The primary endpoint was the percent change from Baseline to Week (W) 48 in spine and hip BMD. Differences in percentage changes from baseline in spine and hip BMD were analyzed using ANCOVA models with treatment as fixed effect and baseline BMD and sex as covariates. Secondary endpoints were HIV-1 RNA <50 copies/mL at W24 and W48 (FDA Snapshot) and adverse events.

Results: Of 166 participants, characteristics were well balanced between E/C/F/TAF and TDF arms with a median age of 65 years (range 60-80) 11% female and 92% White. Baseline regimens consisted of 2 NRTIs combined with an NNRTI 78% (130/166), INSTI 12% (20/166), or boosted PI 9.6% (16/166).

BMD (mean percent change from baseline) increased in E/C/F/TAF group and decreased in TDF group at both W24 and W48. At W48, spine BMD increased +2.2% and decreased –0.1% ($p< 0.001$ for between group comparisons) and hip BMD increased +1.3% and decreased –0.7% ($p< 0.001$) in the E/C/F/TAF and TDF groups, respectively. At W48, more patients who switched to E/C/F/TAF had normal hip T scores (> -1.0; at baseline 51% and at W48 58%), compared to continued TDF (at baseline 51% and at W48 46%).

At W48, HIV RNA <50 copies/mL was maintained in 94% of participants in both arms. Confirmed HIV RNA >50 copies/mL was found in 1 participant in each arm; neither had drug resistance. There were no study-drug related Grade 3-4 AEs. AEs leading to premature study drug discontinuation were similar: 3.6% with E/C/F/TAF and 1.8% with TDF.

Conclusion: Through W48, spine and hip BMD significantly increased in older participants who switched to E/C/F/TAF compared to those who continued a TDF-containing regimen. HIV-1 RNA suppression was maintained through W48. The W48 BMD, safety and efficacy data support the switch to E/C/F/TAF in suppressed HIV-infected participants aged ≥60 years.

#9

High level of pre-existing nrti resistance prior to switching to b/f/taf (study 4030)

Acosta R[1], Willkom M[1], Andreatta K[1], Liu H[1], Martin R[1], Chang S[1], Martin H[1], Collins S[1], Zheng T[2], White KL[1]

[1]Gilead Sciences, Inc, Foster City, CA, USA, [2]Gilead Sciences, Ltd, Shanghai, China

Background: Bictegravir (B) is coformulated with the nucleoside/tide reverse transcriptase inhibitors (NRTIs) emtricitabine (F) and tenofovir alafenamide fumarate (TAF) (B/F/TAF). Study 4030 is an ongoing, fully enrolled, phase 3, randomized, double-blinded study (n=565) of HIV-1 RNA suppressed participants on QD dolutegravir (DTG) + F/TAF or F/tenofovir disoproxil fumarate (TDF) switching 1:1 to DTG + F/TAF or B/F/TAF for 48 weeks. Documented INSTI resistance was not enrolled if known at randomization, but all NRTI, NNRTI, and PI resistance was allowed.

Methods: Proviral DNA genotypes (GenoSure Archive) from baseline samples and historical plasma HIV-1 RNA genotypes were analyzed. Documented or suspected NRTI resistance was assigned to group 1) K65R/E/N or ≥3 TAMs containing M41L or L210W (TAMs: D67N, K70R, L210W, T215F/Y, and K219Q/E/N/R), group 2) M184I/V, any other set of TAMs, K70E/G/M/Q/S/T, L74I/V, V75A/S/M/T, Y115F, T69D, or Q151M, or group 3) no major NRTI resistance. Virologic outcomes used last available on-treatment HIV-1 RNA with the blinded Week 12 IDMC data cut.

Results: Historical genotypes were available from 285/565 participants (50%). Retrospective analysis of archived mutations by HIV DNA genotype were determined for 377/565 participants; 200 also had historical genotypes. In total, 82% (462/565) of participants had pre-switch genotypic data available resulting in 24% with major NRTI resistance: 5% (29/565) in group 1 (K65R or ≥3TAMs) and 18% (104/565) in group 2 (other NRTI mutations). M184V/I was present in 17% (77/462) of participants with data. HIV DNA genotyping identified previously unknown major NRTI resistance in 15% of participants (58/377). Pre-existing INSTI mutations were found in 5% of participants (19/399): T97A (n=12), N155S (N=1), Y143H (n=2), R263K (n=2), Q148H+G140S (n=1), and S147G (n=1). Primary non-nucleoside RT inhibitor and protease inhibitor resistance mutations were present in 24% (113/462) and 8% (36/462) of participants. At this interim analysis, HIV-1 RNA <50 copies/mL was maintained in 99% of participants, 97% (28/29) in group 1, 99% (103/104) in group 2, 97% (75/77) with M184V/I, and 100% (19/19) with INSTI-R.

Conclusion: This study found frequent NRTI resistance in suppressed participants switching from a DTG + F/TDF or F/TAF regimen, much of which was previously undocumented. Early data show high suppression using potent triple therapy of B/F/TAF or DTG + F/TAF.

#10

基于 PI 和 DTG 的二联疗法与基于 PI 和 INI 的三联疗法失败在无既往病毒学失败的 HIV 患者中的临床结局

Calvez V, Armenia D, Charpentier C, Santoro M, Soulie C, Wirden M, Perno C, Descamps D, Ceccherini-Silberstein F, Marcelin AG

Sorbonne University Inserm U1136 Virology paris France, Tor Vergata University Virology Rome Italy, Sorbonne Paris Cité, Inserm IAME, UMR 1137 Virology paris France, University of Milan Virology Milan Italy

背景：指南推荐 HIV 患者在初始治疗中使用三联疗法（TT），而对于更换治疗方案的患者而言，近期一些欧洲指南将部分二联疗法（2DC）列入其中，作为替代方案，用于病毒达到抑制患者的维持治疗。既往有研究表明，与大多数 TT 相比，2DC 用于常规实践时，病毒学失败（VF）的患者出现更多的耐药病例。本研究的目的是对比基于整合酶抑制剂（INI）或蛋白酶抑制剂（PI）的 TT 失败与 2DC 失败在无既往 VF 的患者中的结局。

材料和方法：在 TT（PI 或 INI）或 2DC（包含 PI 和/或 DTG 的方案）失败的患者中，在第一次 VF 时进行基因型耐药检测。病毒学失败的定义为连续两次 HIV 血浆病毒载量> 50 拷贝/ml。研究纳入了 100 名基于 INI 的 TT（RAL、EVG / cobi、DTG）失败的患者以及 100 名基于 PI 的 TT（DRV/r ATV/r）失败的患者（数据库中的连续数据），而且所有符合条件的患者或是基于 DTG 的 2DC （DTG + 3TC，DTG + RPV）失败，或是基于 PI 的 2DC（PI + RAL，DTG 或 3TC）失败。基因型检测的研究时间为 2015-2018 年。

结果：基于 DTG 的 2DC 组中纳入了 23 名已经出现过第一次病毒学失败的患者，基于 PI 的 2DC 组中纳入了 32 名。TT 组的中位年龄为 39 岁，2DC 组为 41 岁；TT 组的既往治疗方案数目中位值为 2，2DC 组为 3；对于中位 VL 最高值，TT 组为 79,239 拷贝/ml，2DC 组为 156,966 拷贝/ml；关于失败时的中位 VL，TT 组为 3,019 拷贝/ml，2DC 组为 4,313 拷贝/ml。3.0%的 PI TT 患者，7.0%的 INI TT 患者（0.0%的基于 DTG 的 TT 患者），21.7%的 DTG 2DC 患者和 37.5%的 PI 2DC 患者在失败后出现耐药。表 1 根据初始治疗方案组汇总了失败后的后续方案的特征（PI 使用%，多片剂方案%）。

结论：与包含 INI 或 PI 的 TT 相比，在包含 DTG 或 PI 的 2DC 失败的患者中观察到更高的耐药率。2DC 患者在失败后转换为更复杂的方案，包含 PI，而且与 TT 失败的患者相比，片剂数目更多。

表 1. 耐药和失败后的后续治疗的特征

	2NRTIs+PI	**2NRTIs+INI**	**基于 DTG 的 2DC**	**基于 PI 的 2DC**
N	100	100	23	32
耐药 %	3.0%	7.0%	21.7%	37.5%
PI 使用 %	3.0%	7.0%	39.1%	65.6%
MTR 使用 %	4.0%	7.0%	52.2%	65.6%

#11

在大型西班牙队列-VCCH 中，HIV 标准三联疗法（TT）的真实世界治疗持久性明显优于二联疗法（DT）

Ramón T, *hospital de Sierrallana, Torrelavega The VACH Study Group* ramon.teira1@gmail.com

目的：治疗持久性和依从性与改善患者预后相关。此外，较长的治疗持久性可能会延缓与更昂贵的后续治疗相关的额外成本。本研究的目的是对比包含整合酶抑制剂（INI）的三联疗法（TT）与二联疗法（DT）的真实世界治疗持久性。

方法：使用来自VACH队列的数据进行了回顾性分析，该队列是一个前瞻性多中心西班牙成人HIV患者队列。在2012年01月01日至2017年06月01日期间，所有开始接受含INI（EVG、RAL、DTG）联合两种NRTI（F/TAF、F/TDF或3TC/ABC）的TT，或包含DTG和/或PI/r的DT的患者均包括在分析中。分析的单位是患者-方案。至非持续性时间（即失败）的定义为从患者-方案开始至治疗停止（由于任何原因）、失访、死亡或截尾之间的时间间隔，以先发生者为准。使用Kaplan-Meier曲线和Cox比例风险模型（控制人口统计学特征、合并症、病毒载量、CD4、既往治疗方案的数目、CD4最低点和接受抗逆转录病毒治疗的年数——均在患者-方案启动时）。

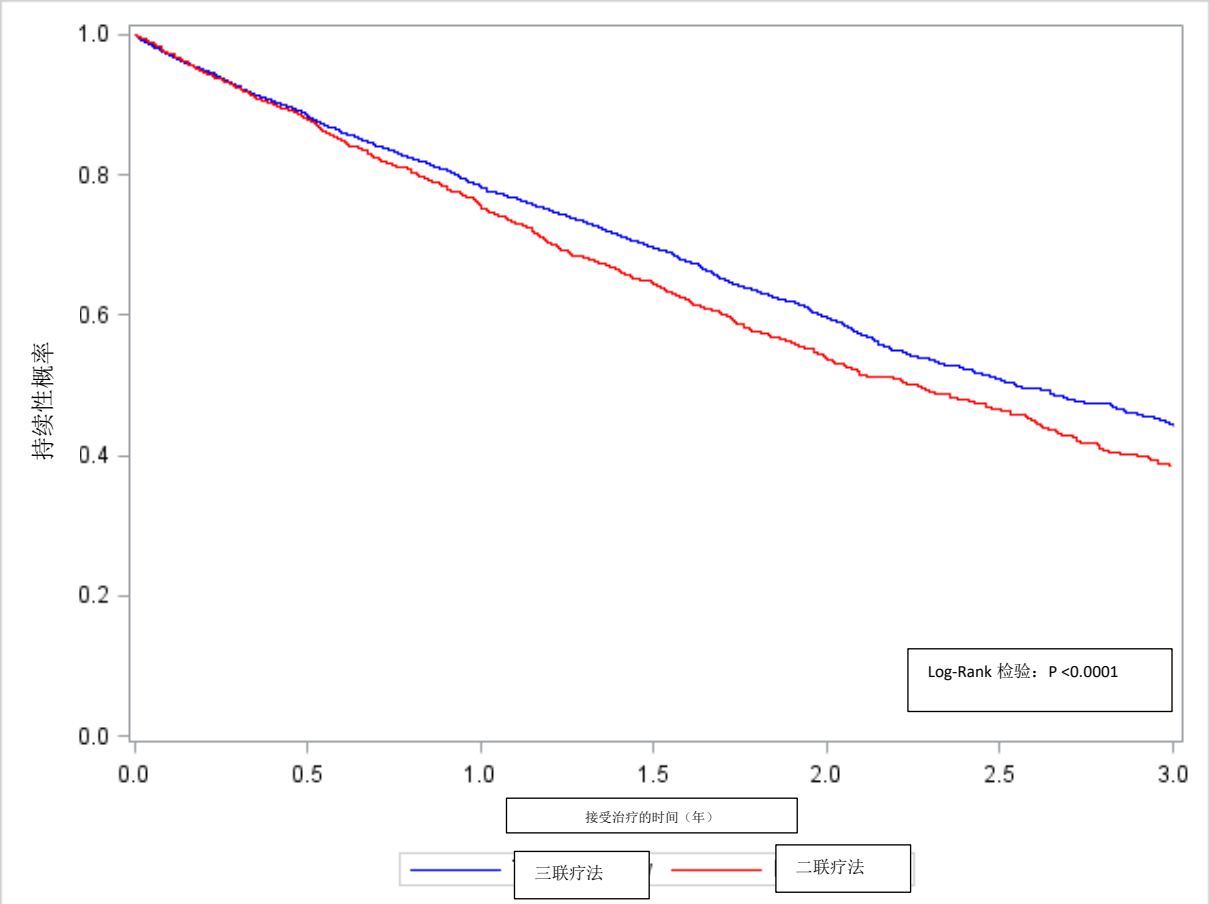
结果：共有7,766个TT和2,178个DT患者-方案。在TT中，最常见的方案是DTG“+或/”ABC/3TC（35.3%）和EVG/c/TAF/FTC（24.6%）。在DT中，42.3%不含INI PI，57.7%包含INI（31.7%DTG，26.0%RAL）。基线患者-方案特征在两组间存在差异（见表1）；DT组的患者年龄更大，而且治疗经验更丰富。TT和DT的中位持续时间分别为2.6和2.3年（见图1，Log-Rank检验：P <0.0001）。当对患者特征间的差异进行控制时，获得的DT与TT的风险比（HR）为1.2 [p = 0.0008]。将队列限制为包含DTG的TT和DT时，等效HR增加至1.4（p = 0.0011）。

结论：与接受基于INI或PI的DT的患者相比，接受基于INI的TT的患者的治疗持久性显著较高。与包含DTG的三联疗法相比，基于DTG的二联疗法停止治疗风险增加了40%。

表 1: 方案开始时的基线患者-方案特征

	三联疗法	二联疗法	P 值
年龄，均值 （SD）	47.3 (10.1)	49.6 (9.1)	<0.0001
诊断时的年龄，均值 （SD）	33.4 (10.2)	32.6 (10.3)	0.006
男性，%	76.8%	72.5%	0.0003
eGFR，均值 （SD）	84.3 (34.4)	83.3 (30.3)	0.22
Framingham CHD 风险评分（中危，高危）	30.4%, 11.7%	31.0%, 17.2%	<0.0001
既往 AIDS 诊断，CD4 最低值 <50	25.1%, 17.3%	33.8%, 25.1%	<0.0001, <0.001
CD4 >500，病毒载量 <50 拷贝/mL	60.0%, 76.9%	58.4%, 72.0%	0.19, <0.001
既往治疗方案的数目，平均值 （SD）	4.4 (3.6)	7.2 (5.3)	<0.0001
接受抗逆转录病毒治疗的年数，平均值 （SD）	11.5 (7.5)	14.5 (7.0)	<0.0001

图 1:



#12

Cumulative safety review of elvitegravir and bictegravir use during pregnancy and risk of neural tube defects

Farrow T[1], Deaton C[1], Nguyen NQ[1], Muramoto D[1], Troostenburg A[1], Ng L[1], Liu L[1], Martin H[1], Lauren Temme[1], Hygieia Liu[2],Moupali Das[1]

[1]Gilead Sciences, Inc, Foster City, CA, USA, [2]Gilead Sciences, Ltd, Shanghai,China

Background: The global prevalence of neural tube defects (NTDs) is estimated to be 0.18% (95% confidence interval: 0.15, 0.23) [1]. Preliminary findings from an ongoing birth outcome surveillance study in Botswana (Tsepamo Study) suggested an increased risk of NTDs in infants born to mothers treated with dolutegravir, an integrase strand transfer inhibitor (INSTI), at the time of conception [2]. Reported pregnancies in the Gilead global safety database were reviewed to evaluate the number of NTD cases and to assess the risk of NTDs associated with exposure to the INSTIs, elvitegravir (EVG) or bictegravir (BIC).

Methods: Cumulative from beginning of clinical development to 31 May 2018, all pregnancy cases reported for women exposed to EVG- and BIC-containing products were retrieved from the Gilead global safety database, which included reports from clinical trials, spontaneous postmarketing reports, and literature review. Given that the exact timing of medication exposure relative to conception is often unconfirmed in spontaneous reports, cases of NTDs diagnosed either anatomically or radiologically were identified regardless of the trimester of exposure. A prevalence rate could not be derived from these data, as many cases originated from retrospective reports, drawn from a population in which the number of exposed pregnancies is unknown [3].

Results: For EVG-containing products, 630 pregnancies were identified. There was one retrospectively identified case of a fetal NTD reported during the pregnancy of a 34-year-old woman in the US who received EVG/cobicistat/emtricitabine (FTC)/tenofovir alafenamide prior to conception and then switched to raltegravir + FTC/tenofovir disoproxil fumarate 48 days post last menstrual period (LMP). An ultrasound 19 weeks post LMP showed anencephaly. Obstetric history, other risk factors for NTD, and folate supplementation were not reported. The pregnancy was ongoing and pending birth outcome.
For BIC-containing products, 25 pregnancy cases were identified. No NTDs were reported.

Conclusions: A search of the Gilead global safety database identified one case of NTD with pending birth outcome in a pregnancy of a woman exposed to EVG prior to conception. Viewed in the context of more than 600 pregnancy cases in women exposed to EVG, this single case cannot be distinguished from the background rate in the general population. Review of the limited data for BIC identified no cases of NTD.

#13

B/F/TAF versus ABC/DTG/3TC or DTG + F/TAF in treatment-naïve adults with high baseline viral load or low baseline CD4 count in 2 Phase 3 randomized, controlled clinical trials: Week 96 Results

Podzamczer [1], Stellbrink H[2], Orkin C[3], Arribas J[4], Koenig E[5], Ramgopal M[6], Baumgarten A[7], Wei XL[8], SenGupta D[9], Li N[10], Martin H[11]

[1]Hospital Universitari de Bellvitge, Barcelona, ES, [2]ICH Study Center Hamburg, DE, [3]Barts Health NHS Trust, Royal London Hospital, Ambrose King Centre, London, UK,[4]Hospital Universitario La Paz, Madrid, ES,[5]Instituto Dominicano de Estudios Virologicos IDEV, Santo Domingo, DM, [6] Midway Immunology and Research Center Fort Pierce, FL, US, [7] Zibp Zentrum fur Infektiologie Berlin Prenzlauer Berg, Berlin, DE, [8,9,11] GSI, Foster City, CA, US, [10] GSI, Shanghai, China

Background: Treatment-naïve, HIV-1-infected individuals with high viral load (HIV-1 RNA) and/or low CD4 count may be difficult to treat. In two Phase 3 studies of fixed-dose combination bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) vs. dolutegravir comparators, there were no treatment differences between arms for subgroups with HIV-1 RNA >100,000 copies (c)/mL or CD4 <200 cells/µL at baseline. B/F/TAF was non-inferior to comparator arms by Shapshot at the primary endpoint, Week (W) 48, and W96. No participant failed with resistance. To further characterise efficacy of B/F/TAF, we analysed pooled results from these trials for those with high viral load or low CD4 count at baseline. Results were similar among treatment groups at W48; herein, we present results at W96.

Materials and Methods: Treatment-naïve, HIV-1-infected adults were randomised 1:1 to receive blinded treatment with B/F/TAF (50/200/25 mg) vs. dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) (Study 1489) or DTG (50 mg) + F/TAF (200/25 mg) (Study 1490). Participants were recruited in North America, Europe, and Australia. To evaluate the real efficacy of B/F/TAF in these populations, we conducted a per-protocol (PP) analysis, which included all participants randomised who received ≥1 dose of study medication but excluded those without on-treatment results in the W96 window (unless discontinued for lack of efficacy) or who had low medication adherence (<2.5th percentile). We present W96 virologic responses by FDA Snapshot algorithm for participants with baseline viral load >100,000 c/mL or CD4 count <200 cells/µL or both using the W96 PP analysis set.

Results: 629 adults were randomised in study 1489 (B/F/TAF n=314, DTG/ABC/3TC n=315) and 645 in study 1490 (B/F/TAF n=320, DTG+F/TAF n=325). Pooled, 184 participants (PP analysis set) had baseline viral load >100,000 copies/mL (B/F/TAF n=95/634 [15%], DTG/ABC/3TC n=43/315 [14%], DTG+F/TAF n=46/325 [14%]), and 122 (B/F/TAF n=65/634 [10%], DTG/ABC/3TC n=26/315 [8%], DTG+F/TAF n=31/325 [10%]) had baseline CD4 count <200 cells/µL. For both high viral load and low CD4 subgroups, virologic suppression (HIV-1 RNA <50 c/mL) at W96 was similarly high for B/F/TAF, DTG/ABC/3TC, and DTG+F/TAF. No participant failed with resistance to any components of study drug.

Conclusions: B/F/TAF demonstrated potent viral suppression with no treatment-emergent resistance in treatment-naïve adults with high baseline viral load and/or low CD4 count through W96. These data provide further evidence that B/F/TAF is an appropriate treatment for a wide range of patients, including late presenters who have been historically more difficult to treat.

#14

大型西班牙队列- VACH 中，标准三联疗法与二联疗法用于病毒载量低于 50 拷贝/ml 的 HIV 经治患者时的真实世界对比

背景：近期，一些欧洲 HIV 治疗指南将部分二联疗法（DT）纳入其中，作为抑制患者的方案更换选择，从而简化治疗方案或者避免副作用。本研究评估了方案更换为三联疗法（TT）或 DT 的病毒载量低于 50 拷贝/ml 的 HIV 经治患者的治疗持久性，以及由于病毒学失败和不良事件导致停止治疗的风险。

材料和方法：使用VACH队列的数据进行了回顾性分析，该队列是一个前瞻性多中心西班牙成人HIV患者队列。所有符合下列条件的经治患者均包括在分析中：在2012年01月01日至2017年06月01日期间，更换为新方案，VL <50拷贝/ ml，限于包含INI（EVG、RAL、DTG）联合NRTI（F/TAF、F/TDF或3TC/ABC）的TT，或者包含DTG和/或PI/r的DT。分析的单位是患者-方案。至非持续性时间的定义为从患者-方案开始至治疗停止（由于任何原因）、失访、死亡或截尾之间的时间间隔，以先发生者为准。使用Kaplan-Meier曲线和Cox比例风险模型（控制人口统计学特征、合并症、CD4、既往治疗方案的数目、CD4最低点和接受抗逆转录病毒治疗的年数——均在患者-方案启动时）。

结果：共纳入了5596个TT和1386个DT患者-方案。在TT中，最常见的治疗方案是DTG联合3TC/ABC（37.0%）和EVG/c/FTC/TAF（27.7%）。在DT中，36.2%包含DTG，73.2%包含PI（9.4%DTG + PI）。至观察期结束时，29.3%的DT方案和22.3%的TT方案已经停止使用。基线患者 - 方案特征在两组间存在差异：DT组的患者年龄更大，而且治疗经验更丰富。当对患者特征间的差异进行控制时，获得的DT与TT由于任何原因停止治疗的风险比（HR）为1.23（p = 0.003），而且由于病毒学失败而停止治疗的HR为1.86（p = 0.01）。未观察到两组在由于不良事件而停止治疗的风险方面存在差异（HR = 1.15，p = 0.29）。

结论：在更换方案时抑制的经治患者中，与接受基于INI或PI的DT的患者相比，在接受基于INI的TT的患者中，治疗持久性显著较高；并且预计DT中的病毒学失败风险高86%。未观察到两组在由于不良事件而停止治疗的风险方面存在差异。

#15

Phase 3 randomized, controlled clinical trial of bictegravir coformulated with FTC/TAF in a fixed-dose combination (B/F/TAF) vs dolutegravir (DTG) + F/TAF in treatment-naïve HIV-1 positive adults: week 96 results

Stellbrink HJ[1], Arribas J[2], Stephens JL[3], Albrecht H[4], Sax PE[5], Maggiolo F[6], Creticos C[7], Martorell CT[8], Wei X[9], White K[9], Collins S[9], Zheng T[10], Martin H[9].

[1]ICH Study Center, Hamburg, DE, [2] Hospital Universitario La Paz, Madrid, Spain, [3] Mercer University School of Medicine, Macon, GA, US, [4] Palmetto Health , Richland, SC, [5] Brigham and Women's Hospital, Boston, MA, [6] Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, IT, [7] Howard Brown Health Center, Chicago, Illinois, [8] Infectious Diseases and The Research Institute, Springfield MA, [9]GSI, Foster City, CA, [10] GSI, Shanghai, China.

Background: Bictegravir (B), a novel, potent integrase strand transfer inhibitor with a high barrier to resistance, is coformulated with emtricitabine (F) and tenofovir alafenamide (TAF) as the European Medicine Agency-approved single-tablet regimen, B/F/TAF. We report Week (W) 96 secondary endpoint results from an ongoing, double-blind, phase 3 study directly comparing B with dolutegravir (DTG), each given with F/TAF in treatment-naïve, HIV-infected adults. Both treatments demonstrated high efficacy with no viral resistance and were well tolerated through W48.

Methods and Methods: 645 treatment-naive adults living with HIV-1 and estimated glomerular filtration rate (eGFR) ≥30 mL/min were randomized 1:1 to receive blinded treatment with B/F/TAF (50/200/25 mg) or DTG (50 mg) + F/TAF (200/25 mg) with matching placebos once daily. Chronic hepatitis B and/or C infection was allowed. Primary endpoint was proportion of participants with HIV-1 RNA <50 copies/mL (c/mL) at W48 (FDA snapshot); same measure of efficacy was evaluated as a secondary endpoint at W96. Noninferiority for the secondary endpoint was assessed through 95% confidence intervals (CI) with 12% margin. Secondary endpoints were safety measures (adverse events [AEs], laboratory results).

Results: At W96, 84.1% (269 of 320) on B/F/TAF and 86.5% (281 of 325) on DTG+F/TAF had HIV-1 RNA <50 c/mL (difference -2.3%; 95%CI -7.9% to 3.2%, p=0.41). Number of participants with HIV-1 RNA ≥50 c/mL at W96 was 0 for B/F/TAF and 5 (1.5%) for DTG+F/TAF. In the per-protocol analysis, 100% of participants on B/F/TAF had HIV-1 RNA <50 c/mL vs. 98.2% on DTG+F/TAF (p=0.03). Through W96, no participant had emergent resistance to study drugs. AEs led to discontinuation in 6 (2%) B/F/TAF vs 5 (2%) DTG+F/TAF (1 [B/F/TAF] and 4 [DTG+F/TAF] after W48). Most common AEs overall were diarrhea (18% B/F/TAF, 16% DTG+F/TAF) and headache (16% B/F/TAF, 15% DTG + F/TAF). Treatment-related AEs were reported for 20% B/F/TAF vs 28% DTG+F/TAF (p=0.02). Lipid changes were not significantly different between groups. No renal discontinuations and no cases of proximal renal tubulopathy were reported.

Conclusions: After 96 weeks, B/F/TAF achieved virologic suppression in 84.1% of treatment-naïve adults with no treatment-emergent resistance, and 100% had HIV-1 RNA <50 c/mL in the per protocol analysis. B/F/TAF was safe and well tolerated with fewer treatment-related AEs compared to DTG+F/TAF.

#16

根据西班牙 VACH 队列的肾脏和心血管疾病的风险特征，预测艾维雷韦、考比司他、恩曲他滨和丙酚替诺福韦（E/c/F/TAF）的健康结果

Teira R[1], Garrido M[2], Folse H[3], Suarez-Lozano I[4]

[1]Hospital de Sierrallana Infectious Diseases, Torrelavega, Spain & AMVACH Association. Spanish VACH Cohort. Huelva, Spain, [2]AMVACH Association. Spanish VACH Cohort. Huelva, Spain, [3]Evidera, San Francisco, CA, USA,[4]Complejo Universitario Hospitalario de Huelva, Hospital Infanta Elena Infectious Diseases, Huelva, Spain

背景：与 TDF 相比，E/c/F/TAF 表现出较高的病毒抑制率，而且肾脏和骨骼安全性标志物显著改善。随着 HIV 感染者的年龄的增长，慢性肾脏疾病（CKD）和心血管疾病（CVD）等合并症的风险和患病率也随之升高。临床试验和真实世界队列中的年龄和合并症风险特征存在显著差异。本分析的目的是预测 E/c/F/TAF 在现实世界西班牙队列中的长期健康结果。

方法：使用先前经验证的成本-后果模型（美国，华盛顿，2016 年 05 月 21 日至 25 日，ISPOR 第 21 届年度国际会议，Gallant，J.等人），在 10,000 名患者的模拟队列中估计 5 年内进展为 CKD-III 和 CVD 事件的患者数目。使用发表的 D：A：D 风险方程中定义的风险特征估计了 CKD-III 和 CVD 事件。输入来自于已发表的随机对照试验和同行评议的文章。使用 VACH 队列的罹患 CKD 和 CVD 的风险分别为低/中/高的患者比例来描述西班牙 HIV +人群中的风险特征。

结果：纳入分析的患者的平均（SD）年龄为 48.0（9.1）岁，其中 43.0%的患者的年龄为 50 岁以上。CKD 的估计风险（低/中/高）为 26.7%/42.7%/30.6%，CVD 为 55.4%/32.0%/12.6%。5 年内，方案更换为 E/c/F/TAF 后，与 GESIDA 推荐的基于 TDF 的治疗方案相比，进展为 CKD 事件的患者比例平均下降 41%；与基于 ABC 的推荐方案相比，CVD 事件的患者比例下降 24%。与接受基于 TDF 的治疗方案的患者相比，在接受 E/c/F/TAF 治疗的患者中，为了避免发生一项进展为 CKD 事件而需要治疗的数目（NNT）平均值为 24；而与继续接受基于 ABC 的治疗方案的患者相比，在接受 E/c/F/TAF 治疗的患者中，为了避免发生一项 CVD 事件的 NNT 为 56。

结论：根据 VACH 队列中观察到的真实世界患者特征，与基于 F/TDF 和 ABC/3TC 的推荐方案相比，预计 E/C/F/TAF 可改善健康结果。

#17

Tenofovir Alafenamide Vs Tenofovir Df In Women: Pooled Analysis Of 7 Clinical Trials

Thompson MA[1], Brar I[2], Brinson C[3], Creticos CM[4], Hagins D[5], Koening E[6], Martorell CT[7], Mussini C[8], Waters L[9], Guo S[10], Liu Y[10], Brainard D[10], Temme L[10], SenGupta D[10], Li N[10], Das M[10]

[1] AIDS Research Consortium of Atlanta, Atlanta, GA, [2] Henry Ford Hospital, Detroit, MI, [3] Central Texas Clinical Research, Austin, TX, [4] Howard Brown Health Center, Chicago, IL, [5] Chatham County Health Department, Savannah, GA, [6] Instituto Dominicano de Estudios, Virologicos, Santo Domingo, Dominican Republic, [7] The Research Institute, Springfield, MA, [8] Mussini C, Azienda Ospedaliera Universitaria Policlinico di Modena, Modena, Italy, [9] Mortimer Market Centre, London, UK, [10] Gilead Sciences

Background: Globally, the majority of people living with HIV are cis-women, who are underrepresented in clinical trials. Tenofovir alafenamide (TAF) has demonstrated an improved renal and bone safety profile relative to tenofovir disoproxil fumarate (TDF) in multiple randomized trials with similar efficacy. We pooled 7 studies to evaluate the efficacy and safety of TAF vs. TDF for ART initiation or switch in women.

Materials & Methods: Data from 779 cis-women in 7 randomized, double-blind clinical trials (2 in treatment-naïve adults, 5 in virologically suppressed adults) through W96 were analyzed. All participants who initiated or switched to TAF-based regimens (elvitegravir/cobicistat/emtricitabine [FTC]/TAF, rilpivirine/FTC/TAF, FTC/TAF, or bictegravir/FTC/TAF) were compared with those who initiated or continued TDF-based regimens. Virologic suppression (VS; HIV-1 RNA <50 c/mL) rates at W96 were determined by FDA snapshot analysis. Bone mineral density (BMD) and the renal tubular biomarkers urine beta-2-microglobulin (B2M):creatinine (Cr) ratio and retinol binding protein (RBP):Cr ratio are reported at W96. Differences were compared using Wilcoxon rank sum test.

Results: A total of 779 cis-women were enrolled (n=429 TAF, n=350 TDF). Participants were primarily women of color (67% black or Hispanic/Latina; 45% black and 25% Hispanic/Latina). Treatment-naïve women (WTN) had a median age of 37 years with median HIV-RNA 4.47 $\log_{10}$ c/mL and CD4 365 cells/mm^3. Women with VS (WVS) had a median age 47 years with median CD4 711 cells/mm^3. Of WTN, 86% (TAF) and 85% (TDF) achieved VS (p=0.71) at W96. VS was maintained in 86% of WVS switching to TAF and 85% continuing TDF (p=0.99). Overall TAF and TDF were well-tolerated. Discontinuation due to adverse event/death was 0% (TAF) vs. 1.6% (TDF) in WTN and 1.3% (TAF) vs. 2.2% (TDF) in WVS. At W96 there was less impact on renal biomarkers in WTN initiating TAF- vs. TDF-based regimens (median % change in RBP:Cr ratio +12.1 vs. +67.5; B2M:Cr ratio -37.4 vs. +13.1; p<0.001 for both), and decreases in BMD were smaller (median % change in spine BMD -0.292 vs. -2.606; hip BMD -1.296 vs. -3.938; p<0.001 for both). Women switching from TDF to TAF experienced decreases in tubular proteinuria (median % change in RBP:Cr ratio +8.0 vs. +50.8; B2M:Cr ratio -9.5 vs. +29.2; p<0.001 for both) and improvements in BMD (median % change in spine BMD +1.703 vs. -1.055; hip BMD +1.699 vs. -0.831; p<0.001 for both) at W96.

Conclusions: Similar to the overall results in pivotal naïve and switch trials of FTC/TAF-based regimens, cis-women who initiated or switched to TAF had significantly improved bone and renal safety parameters compared to TDF, with similar rates of virologic suppression through W96. These pooled data from 7 studies demonstrate a safety advantage for initiating therapy with or switching to TAF compared to TDF in women.

#18
伴和不伴 HIV 的美国退伍军人中的重症抑郁和自杀意念的发生率和风险

Sutton SS[1,2] , Magagnoli J[2], Hardin JW[2,3], Beaubrun A[4] , Hsu L[4], Edun B[2], Cummings TH[2]

[1] Department of Clinical Pharmacy and Outcomes Sciences, University of South Carolina, College of Pharmacy, Columbia, South Carolina, [2] WJB Dorn Veterans Affairs Medical Center, Dorn Research Institute, Columbia, South Carolina, [3] Department of Epidemiology and Biostatistics, University of South Carolina, Norman J. Arnold School of Public Health, Columbia, South Carolina,[4] Gilead Sciences Inc, Foster City, CA, USA

背景：神经精神疾病仍然是 HIV 患者中观察到的重要合并症。本研究的目的是使用退伍军人事务部（VA）管理系统的数据，提供当前针对匹配的伴和不伴 HIV 的退伍军人队列中的抑郁症和自杀意念的发生率和风险的估计值。

材料和方法：从退伍军人事务部信息科学和计算基础设施（VINCI）获取回顾性索赔数据，其中包括人口统计学特征、行政索赔和药房配药数据。通过 ICD-9/10 代码确定于 2001 年 01 月至 2017 年 12 月期间确诊的 HIV 病例，并将 HIV 诊断日期定义为指示日。根据 VA 的出生年份、种族、性别和入伍年份，匹配对照组的病例。要求 HIV 病例和对照组在指示日之前至少有一年时间的数据，并且在指数年中至少有 60 天的随访时间。要求对照组与其匹配的 HIV 患者的医疗索赔年份相同，而且将对照组的指示日设定为与其病例相同的指示日。同样地，通过 ICD-9/10 代码确定了自杀意念/尝试和重症抑郁。新发病例的定义为在住院或门诊环境下得到确诊的病例，其中之前的 12 个月未诊断出关注的疾病。根据泊松分布计算具有 95%置信区间（CI）的每 1000 人年（PY）的发生率。为了测量 HIV 状态与自杀意念和重症抑郁之间的关系，计算了使用广义估计方程（GEE）估计的泊松模型的相对风险，调整了基线和临床特征。

结果：样本包括 19,413 名 HIV 患者（平均年龄 50.6 岁；97.2%男性；49.9%黑人，39.8%白人，10.3%其他种族或种族不详）和 19,413 名具有相似人口统计学特征的匹配对照患者。 2017 年的重症抑郁的发生率在 HIV 病例中约为 40.8 例每 1000 PY（95%CI：36.8-45.1），在匹配的对照组中为 26.7 例每 1000 PY（95%CI：23.9-29.7）。自杀意念的发生率在 HIV 病例中约为 5.6 例每 1000 PY（95%CI：4.4-7.0），在匹配的对照组中为 2.8 例每 1000 PY（95%CI：2.0-3.7）。在控制基线协变量后，与匹配的非 HIV 对照组相比，HIV 与重症抑郁的风险增加 21%相关（RR 1.21,95%CI：1.09-1.35），并且与自杀意念/尝试风险增加超过两倍相关（RR 2.79 95%CI：1.94-4.01）。

结论：在大型回顾性队列中，与无 HIV 的匹配对照组相比，感染 HIV 的退伍军人罹患重症抑郁和出现自杀意念的风险更高。神经精神疾病的风险应被视为与治疗相关，而且应评估其他干预措施用于 HIV 患者时的效果。

#19

A Phase 3, Randomized, Controlled Clinical Trial of Bictegravir in a Fixed-Dose Combination, B/F/TAF, vs ABC/DTG/3TC in Treatment-Naïve Adults at Week 96

Wohl D[1], Yazdanpanah Y[2], Baumgarten A[3], Clarke A[4], Hagins D[5], Ramgopal MN[6], Wei X[7], White K[7], Collins S[7], Li N[8], Martin H[7]

1University of North Carolina at Chapel Hill, Chapel Hill, NC. 2Hôpital Bichat Claude Bernard, Paris. FR, 3 Zentrum für Infektiologie Berlin Prenzlauer Berg (ZIBP), Berlin, DE, 4 Royal Sussex County Hospital, Brighton, UK, 5 Georgia Department of Public Health, Coastal Health District, Chatham Care Center, Savannah, GA, 6 Midway Immunology Center, Ft. Pierce, FL, 7 GSI, Foster City, CA, 8 GSI, Shanghai, China

Introduction: Bictegravir (B), a potent INSTI with a high barrier to resistance, is coformulated with emtricitabine (F) and tenofovir alafenamide (TAF) as the FDA-approved single-tablet regimen B/F/TAF. We report Week (W) 96 results from an ongoing phase 3 study comparing B/F/TAF to coformulated dolutegravir, abacavir, and lamivudine (DTG/ABC/3TC) in treatment- naïve adults living with HIV-1. Primary outcome at W48 demonstrated noninferior virologic responses, similar bone and renal profiles, and no viral resistance.

Methods: We randomized 1:1 HLA-B*5701-negative adults, without HBV and with estimated glomerular filtration rate (eGFR) ≥50 mL/min to receive blinded B/F/TAF (50/200/25 mg) or DTG/ABC/3TC (50/600/300 mg) with matching placebos QD. Primary endpoint was proportion with HIV-1 RNA <50 c/mL at W48 (FDA snapshot), with secondary analyses at W96. Noninferiority was assessed with 95% confidence intervals (CI) (12% margin). Other secondary endpoints were safety (adverse events [AEs], laboratory abnormalities) and predefined analyses of bone mineral density (BMD) and measures of renal function (eGFR, proteinuria).

Results: 629 adults were randomized/treated (314 B/F/TAF, 315 DTG/ABC/3TC). At W96, B/F/TAF was noninferior to DTG/ABC/3TC: 87.9% vs 89.8%, respectively, achieved HIV-1 RNA <50 c/mL (difference -1.9%; 95%CI -6.9% to 3.1%, p=0.45). In per-protocol analysis, 99.6% on B/F/TAF vs 98.9% on DTG/ABC/3TC achieved HIV-1 RNA <50c/mL (p=0.33). Most common AEs overall were nausea (11% B/F/TAF, 24% DTG/ABC/3TC, p<0.001), diarrhea (15%, 16%), and headache (13%, 16%). Through W96, no participant had emergent resistance to study drugs. No participant discontinued B/F/TAF due to AEs; 5 (2%) discontinued DTG/ABC/3TC due to AEs (1 after W48). Treatment-related AEs occurred in 28% B/F/TAF vs 40% DTG/ABC/3TC (p=0.002); most common was nausea (6%, 17%. p<0.001). At W96, mean % changes in spine and hip BMD were small and similar between groups (table); median change in eGFR was significantly less with B/F/TAF, while median % changes in proteinuria were similar.

Conclusions: At W96, B/F/TAF was virologically noninferior to DTG/ABC/3TC, with no viral resistance or safety-related discontinuations. B/F/TAF was well tolerated with less nausea than DTG/ABC/3TC and similar bone and renal safety.