**Table.** Hepatic Safety Parameters in Participants with HIV/HCV Co-infection and HIV Mono-infection Receiving CAB + RPV LA Q4W or Q8W through Week 48 in ATLAS-2M

| Liver abnormality, n (%) | HIV/HCV co-infection (N=10) | HIV mono-infection (N=1035)[a] |
|---|---|---|
| ALT ≥3 × ULN | 0 | 18 (2) |
| ALT ≥3 × ULN, BIL ≥2 × ULN, and ALP <2 × ULN | 0 | 3 (<1) |
| Hepatocellular injury[b] | 0 | 15 (1) |
| Hepatocellular injury and BIL ≥2 × ULN | 0 | 3 (<1) |
| Liver stopping event | 0 | 4 (<1)[c] |

ALP, alkaline phosphatase; ALT, alanine aminotransferase; BIL, bilirubin; CAB, cabotegravir; HCV, hepatitis C virus; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; ULN, upper limit of normal.
[a]N=1031 for laboratory abnormalities. [b]Defined as ([ALT/ALT ULN]/[ALP/ALP ULN]) ≥5 and ALT ≥3 × ULN. ALT and ALP must be measured on the same day. [c]All liver stopping events occurred after treatment started. Events included acute hepatitis B virus infection (n=2; both participants withdrew from the study), acute hepatitis E virus infection (n=1; continued CAB + RPV LA dosing), and acute hepatitis C virus infection (n=1; continued CAB + RPV LA dosing; not resolved).

***Conclusion.*** CAB + RPV LA was effective and well tolerated in this small cohort of participants with HIV and asymptomatic HCV co-infection.

***Disclosures.*** **Ronald D'Amico, DO, MSc**, **GlaxoSmithKline** (Shareholder)**ViiV Healthcare** (Employee) **Paul Benn, MB ChB FRCP**, **ViiV Healthcare** (Employee) **Shanker Thiagarajah, MB ChB**, **GlaxoSmithKline** (Employee, Shareholder) **Susan L. Ford, PharmD**, **GlaxoSmithKline** (Shareholder)**ViiV Healthcare** (Employee) **Eileen Birmingham, MD, MPH**, **Janssen Research and Development** (Employee, Shareholder) **Ojesh R. Upadhyay, MPH, MBA**, **GlaxoSmithKline** (Employee) **Louise Garside, PhD**, **GlaxoSmithKline** (Employee) **Rodica Van Solingen-Ristea, MD**, **Janssen Research and Development** (Employee)**ViiV Healthcare** (Employee) **Kati Vandermeulen, M.SC.**, **Janssen Research and Development** (Employee) **William Spreen, PharmD**, **GlaxoSmithKline** (Shareholder)**ViiV Healthcare** (Employee)

## 834. Characterization of Heavily Treatment Experienced HIV-1 Infected Clinical Trial Participants Infected with SARS-CoV-2 COVID 19: Fostemsavir BRIGHTE Phase 3 Clinical Trial

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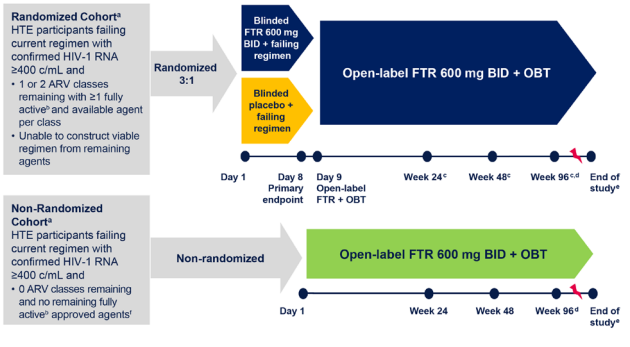
**Session:** P-46. HIV: Complications and Co-infections

***Background.*** BRIGHTE is an ongoing global study evaluating the gp120 attachment inhibitor fostemsavir (FTR) in heavily treatment-experienced (HTE) adults with multidrug resistant (MDR) HIV-1 unable to form a viable antiretroviral (ARV) regimen. An estimated 2 million people living with HIV-1 have been infected with SARS-CoV-2. Those with HIV viremia and/or low CD4+ counts are at increased risk of serious adverse outcome. We describe the reported COVID cases in a clinical trial population of people living with MDR HIV and immune suppression.

***Methods.*** At the start of the COVID pandemic, all ongoing BRIGHTE subjects had achieved ≥ 192 weeks on FTR and optimized background ARVs; results through Week 96 were presented previously. Investigators used WHO guidelines for COVID diagnosis and reported exposure, testing results and symptom presence.

Figure 1. BRIGHTE Study Design




[a]There were no screening TMR $IC_{95}$ criteria. [b]Fully active = no current or historical evidence of resistance and the participant is tolerant of, eligible for, and willing to take (in the case of enfuvirtide) the ARV. [c]Measured from the start of open-label FTR 600 mg BID + OBT. [d]Week 96 database lock August 14, 2018. [e]The study is expected to be conducted until an additional option, rollover study, or marketing approval is in place. [f]Use of investigational agents as part of OBT was permitted.
Bolt symbol, onset of COVID-19 pandemic; ARV, antiretroviral; BID, twice daily; HTE, heavily treatment experienced; OBT, optimized background therapy.

***Results.*** 371 subjects [272 Randomized Cohort (RC), 99 Non-Randomized Cohort (NC)] were enrolled; 44% were ≥ 50 years of age and 86% had an AIDS history. Median CD4+ count at study start of was 80 cells/mm$^3$ (IQR 11–202); 30% with ≤ 20 cells/mm$^3$. 250 subjects remained in BRIGHTE at pandemic start. By April 2021, 17 subjects (14 RC, 3 NC) had confirmed COVID infection (positive PCR test). Severity was Grade 1-3, all cases resolved with no deaths. Six subjects were hospitalized (Table 1); most recent CD4+ count prior to COVID were 293-1641 cells/mm$^3$ and 5/6 subjects were virologically suppressed. Treatments often included prophylactic anticoagulants and supplemental oxygen; no cART changes were made. The remaining 11/17 confirmed cases were managed outpatient. Five more subjects had suspect COVID not confirmed by PCR and 2 subjects had negative PCR tests.

Table 1. Characterization of Participants with Serious AEs of Confirmed COVID-19 Infections – All Hospitalizations

| Participant/ Treatment Cohort | Demographics and Baseline<br>Age (years) / Gender / Race<br>Country<br>CD4+ (cells/mm$^3$) / HIV-1 RNA (c/mL) | COVID Case<br>Positive COVID Test Date / Event Duration / Severity Grade / Outcome<br>Relevant medical history or known exposure risks<br>Pre COVID CD4+ (cells/mm$^3$) and HIV-1 RNA (c/mL)<br>Reported Treatment |
|---|---|---|
| 00376/ Randomized Cohort | 54 / Female / Black<br>Brazil<br>75 cells/mm$^3$, 82,270 c/mL | 15 Apr 2020 / 16 days / Grade 3 / Recovered<br>HIV-1, diabetes, systemic arterial hypertension, no known exposure<br>823 cells/mm$^3$, <40 c/mL<br>ceftriaxone IV, azithromycin, oseltamivir, cefuroxime, enoxaparin, supplemental oxygen via nasal catheter |
| 00631/ Randomized Cohort | 47 / Male / Other (Mestizo)<br>Peru<br>196 cells/mm$^3$, 25,694 c/mL | 24 May 2020 / 19 days / Grade 3 / Recovered<br>HIV-1, systemic arterial hypertension, obesity, recent exposure in community<br>293 cells/mm$^3$, <40 c/mL<br>Orphenadrine, acetaminophen, enoxaparin, albuterol, ipratropium |
| 00626/ Randomized Cohort | 38 / Male / White<br>Argentina<br>131 cells/mm$^3$, 373,289 c/mL | 07 Jul 2020 /19 days / Grade 2 / Recovered<br>HIV-1, smoker, no known exposure<br>876 cells/mm$^3$, <40 c/mL<br>Enoxaparin, omeprazole |
| 00312/ Randomized Cohort | 71 / Male / Black<br>Belgium<br>207 cells/mm$^3$, 2,395 c/mL | 26 Oct 2020 /15 days / Grade 3 / Recovered<br>HIV-1, chronic renal failure/dialysis, recent visit to healthcare facility<br>310 cells/mm$^3$, <40 c/mL<br>Dexamethasone, enoxaparin, aspirin, tramadol, movicol, furosemide, bilastine, darbepoetin alfa, valproic acid, potassium, sodium bicarbonate, calcium carbonate, supplemental oxygen via nasal canula |
| 00524/ Randomized Cohort | 55 / Male / Other (Mulatto)<br>Brazil<br>7 cells/mm$^3$, 112,343 c/mL | 12 Feb 2021 /17 days / Grade 3 / Recovered<br>HIV-1, systemic arterial hypertension, recent exposure in community<br>563 cells/mm$^3$, 117 c/mL<br>Ceftriaxone, ciprofloxacin, dexamethasone, enoxaparine, loperadmide, oxygen support |
| 00449/ Randomized Cohort | 55 / Female / White<br>Brazil<br>368 cells/mm$^3$, 54,925 c/mL | 09 Mar 2021 /43 days / Grade 2 / Recovered<br>HIV-1, asthma, recent exposure in community + visit to healthcare facility<br>1641 cells/mm$^3$, <40 c/mL<br>Dexamethasone, oxygen support |

***Conclusion.*** A total of 22/250 COVID-19 cases (17 confirmed, 5 unconfirmed) have been reported in BRIGHTE. Outcomes were reassuring with no deaths or known persistent sequelae, despite having advanced HIV and comorbid diseases at baseline associated with poorer COVID outcomes. Outcomes may have benefitted from immunologic improvement during the trial.

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## 835. Improvement in Diet Attenuates Antiretroviral Therapy (ART) Associated Weight Gain in Persons with Human Immunodeficiency Virus (PWH)

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**Session:** P-46. HIV: Complications and Co-infections

***Background.*** Weight gain among PWH on ART is a growing clinical concern. We explore factors associated with weight gain at The Ohio State University Wexner Medical Center Infectious Diseases Clinic.

***Methods.*** This was a single-center, retrospective, cohort study of adult PWH on ART for at least 3 months seen at our clinic from 1/1/2015 to 1/1/2019. Patients with CD4+ T cell count < 200 cells/mm$^3$, viral load >200 copies/mL, history of malignancy, or pregnancy were excluded. 870 patients met criteria. Patient demographics, lifestyle factors, medical co-morbidities, concurrent medications, and ART regimens were documented during the study period. The primary outcome was percent weight change over the follow up period. Secondary outcome was the odds of > 5kg weight gain over the study period. The effects of concurrent medications, medical comorbidities, ART combinations, and self-reported lifestyle behaviors on these outcomes were modeled using mixed effect linear and logistic regression analysis.

***Results.*** At baseline, 83.6% were male, 29.2% were African American, and 65.6% had a body mass index ≥ 25 kg/m. Over a mean follow up of 1.86 years, the study population gained a mean percent weight of 2.12 ± 0.21% (p< 0.001) with an odds of weight gain >5kg of 0.293 (p< 0.001). Male sex and increasing age were significantly associated with a decrease in percent weight over the study period as reflected in the table below. Diet was also significantly associated with a decrease in percent weight change over the study period of -1.99 ± 0.47 %, p= < 0.001 and a lower odds of > 5kg of weight gain (OR= 0.70, 95% CI= 0.50 – 0.97, p=0.03). In regression models, combination therapy with tenofovir alafenamide (TAF) and integrase strand transfer inhibitor (INSTI) containing regimens were significantly associated with an increase in percent weight over the study period. Other significant factors including demographics and ART regimens are noted in Table 1.

Table 1. Multivariable Regression Models*

**Table 1:**

| | Percent Change in Weight Over The Study Period | P - Value | Odds Ratio of ≥ 5 kg Weight Gain Over The Study Period | P-Value |
|---|---|---|---|---|
| **Demographic Factors** | | | | |
| Years on regimen (per year) | 0.56 ± 0.22 % | 0.012 | 1.39 (1.20 – 1.61) | < 0.001 |
| Age (per 10 years) | -0.68 ± 0.18 % | < 0.001 | 0.77 (0.69 – 0.87) | < 0.001 |
| Male gender | -1.32 ± 0.56 % | 0.017 | 0.59 (0.42 – 0.83) | 0.003 |
| Diet | -1.99 ± 0.47 % | < 0.001 | 0.70 (0.50 – 0.97) | 0.03 |
| **Antiretroviral Agents** | | | | |
| Darunavir/Ritonavir | - 1.67 ± 0.76 % | 0.027 | 0.55 (0.31 – 1.00) | 0.05 |
| Efavirenz | - 1.62 ± 0.45 % | < 0.001 | 0.65 (0.47 – 0.91) | 0.01 |
| Dolutegravir | 0.97 ± 0.43 % | 0.024 | 1.36 (1.02 – 1.80) | 0.035 |
| Tenofovir Alafenamide/ Emtricitabine | 2.14 ± 0.45 % | < 0.001 | 2.06 (1.48 – 2.87) | < 0.001 |
| Tenofovir Disoproxyl Fumarate/ Emtricitabine | -1.42 ± 0.38 % | < 0.001 | 0.55 (0.41 – 0.73) | < 0.001 |
| Integrase Strand Transfer Inhibitor | 1.09 ± 0.39% | 0.005 | 1.35 (1.02 – 1.77) | 0.03 |
| **Combination ART** | | | | |
| Efavirenz/ Tenofovir Disoproxyl Fumarate/ Emtricitabine | -1.70 ± 0.47 | < 0.001 | 0.59 (0.41 – 0.83) | 0.003 |
| Elvitegravir/ Cobicistat/ Tenofovir Disoproxyl Fumarate/ Emtricitabine | -1.73 ± 1.06 | 0.10 | 0.82 (0.38 – 1.75) | 0.60 |
| Elvitegravir/ Cobicistat/ Tenofovir Alafenamide/ Emtricitabine | 1.97 ± 0.75 | 0.009 | 1.41 (0.87 – 2.30) | 0.17 |
| Dolutegravir/ Tenofovir Alafenamide/ Emtricitabine | 2.07 ± 0.81 | 0.011 | 1.90 (1.13 – 3.18) | 0.015 |
| Non-Nucleoside Reverse Transcriptase Inhibitor/ Tenofovir Disoproxyl Fumarate/ Emtricitabine | -1.49 ± 0.44 | 0.001 | 0.57 (0.41 – 0.79) | 0.001 |
| Non-Nucleoside Reverse Transcriptase Inhibitor/ Tenofovir Alafenamide/ Emtricitabine | 1.53 ± 0.76 | 0.044 | 2.18 (1.32 – 3.58) | 0.002 |
| Integrase Strand Transfer Inhibitor/ Tenofovir Disoproxyl Fumarate/ Emtricitabine | -0.56 ± 0.61 | 0.37 | 0.74 (0.47 – 1.15) | 0.18 |
| Integrase Strand Transfer Inhibitor/ Tenofovir Alafenamide/ Emtricitabine | 2.34 ± 0.54 | < 0.001 | 1.84 (1.29 – 2.62) | 0.001 |

*All models included terms for years in study, age, gender, and weight at study entry

***Conclusion.*** Weight gain in PWH is multifactorial. Key factors associated with weight gain include combination therapy with TAF, particularly when combined with an INSTI. This data highlights the influential role of diet in PWH at risk of ART-associated weight gain.

***Disclosures.*** **Carlos Malvestutto, M.D.**, **Lilly** (Scientific Research Study Investigator)**Regeneron Inc.** (Scientific Research Study Investigator)**ViiV Healthcare** (Advisor or Review Panel member)

### 836. Significant Elevations in CD4$^+$ Count, Post-treatment of Chronic Hepatitis C (HCV) with Direct Acting Antivirals (DAAs), in Human Immune Deficiency, HIV/HCV Co-infected Patients with Prolonged CD4+ lymphocytopenia, despite undetectable HIV RNA

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**Session:** P-46. HIV: Complications and Co-infections

***Background.*** Introduction of DAAs has revolutionized HCV therapy. Treatment of HIV/HCV co-infected patients is challenging and HCV treatment data on this group of patients are limited. **Aim: T**o review pre-and post-DAA treatment parameters, identify measures to improve recruitment and improve quality of care in co-infected veterans. A QC/QI project.

***Methods.*** A retrospective chart review of HIV/HCV co-infected patients treated for HCV with DAA at Detroit VAMC was performed. All patients were on anti-retroviral treatment for HIV with undetectable viral loads. Pre-and post-DAA treatment parameters were compared in patients who completed 12 weeks of treatment. Drug interactions, SVR, CD4+ counts AST, ALT, albumin, INR, platelets, creatinine, alpha-fetoprotein (AFP), HCV RNA, and FIB-4 score were recorded. Pearson correlation coefficient was used for data analysis.

***Results.*** Out of 46 patients, 4 died and 20 were ineligible due to non-compliance, mental illness, or drug use; 22 eligible patients, who had well controlled HIV, received DAAs for 12 weeks. (Genotype was 1a in 14, 1b in 7 and 2b in 1 patient). Compliance rate was 100%, 21 patients were HCV treatment naïve, 1 treated with interferon in the past) and all 22 patients achieved SVR by 12 weeks (in 2 weeks), including patients (n=12) on long term opioids and/or mental health treatment. Among 10/24 patients who showed a significant increase in CD4+ (range > 100 to 400 within 6 months), 8 were cirrhotic and had received DAA + RIB therapy. HIV therapy regimen change to alafenamide combination was required in 7/22 patients, for renal dysfunction. There were decreases in AST/ALT, but no changes in FIB-4 score, platelets, albumin, creatinine, or AFP were noted.

***Conclusion.*** HIV/HCV Co-infected patients who received DAA + RIB had a significant increase in CD4+ lymphocyte counts ($p< 0.05$) (unlike interferon-based regimen). Chronic opioid use and mental health treatment were not a hindrance to successful therapy. The clinical impact of our findings on long-term complications including cirrhosis, hepatocellular carcinoma, and extra-hepatic manifestations of HCV remain to be seen. Recognition of positive predictive markers will delineate the cohort of co-infected veterans who would benefit from DAA therapy beyond HCV eradication.

***Disclosures.*** **All Authors**: No reported disclosures

### 837. Performance of Blood (1- >3)-β-D-Glucan in People with AIDS Presenting with Respiratory Symptoms

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**Session:** P-46. HIV: Complications and Co-infections

***Background.*** The gold standard for diagnosis of *Pneumocystis jirovecii* pneumonia (PCP) is direct visualization of the microorganism in respiratory samples, usually obtained via bronchoalveolar lavage (BAL). Blood β-D-glucan (BDG) is used as a non-invasive adjunctive diagnostic test for PCP, but specificity is only modest, in part because other opportunistic fungal infections cause high BDG. We previously showed BDG-positivity in 94% of people with AIDS (PWA), progressive disseminated histoplasmosis (PDH), and respiratory symptoms in our hospital. In this study, we aim to assess the performance of BDG as a diagnostic test for PCP in PWA who have respiratory symptoms.

***Methods.*** We retrospectively identified PWA who had a BDG result between 2014 and 2019. AIDS was defined as past or current absolute CD4 count < 200 cells/μL, or a past or current AIDS-defining condition. Positive cytological or histological evidence of *P. jirovecii* in bronchoalveolar lavage (BAL) fluid or lung biopsy, or positive *Pneumocystis* PCR on sputum or BAL confirmed PCP. The Fungitell Assay (Associates of Cape Cod, East Falmouth, MA) determined BDG levels as follows: negative, < 60 pg/mL; indeterminate, 60-79 pg/mL, and positive, ≥ 80 pg/mL. Values < 31 pg/mL and those >500 pg/mL were censored at 30 pg/mL and 500 pg/mL, respectively. Respiratory symptoms were defined as cough, dyspnea, chest pain, or hypoxia. We compared BDG results for participants with proven PCP and participants without proven PCP.

***Results.*** We identified 260 PWA with a BDG result, of whom 183 had at least one respiratory symptom. 84 (45.9%) of these participants had a positive BDG. BDG results among participants with and without PCP are shown in Table 1. Of the 44 participants with a positive BDG who did not have PCP, 29 (65.9%) had PDH. Other diagnoses included cryptococcosis and candidemia. The test performance of BDG for the diagnosis of PCP is shown in Table 2. Exclusion of participants with PDH increased the specificity of BDG for PCP to 86.4%.

Table 1. Results of (1->3)-β-D-glucan Testing by Pneumocystis jirovecii Pneumonia Diagnosis Among Participants with AIDS and Respiratory Symptoms

| BDG (pg/mL) | PCP (N=41) | Not PCP (N=142) | P Value |
|---|---|---|---|
| Mean (SD) | 440.3 (± 134) | 127.9 (± 168.8) | |
| Median (Q1, Q3) | 500 (489, 500) | 34.5 (31, 109) | <0.00001[a] |
| Positive BDG ≥80 pg/mL | 40 (97.5%) | 44 (30.9%) | <0.00001[b] |
| Negative BDG <80 pg/mL | 1 (2.4%) | 98 (69.01%) | |
| BDG ≥500 pg/mL | 31 (75.6%) | 19 (13%) | <0.00001[b] |

Data are presented as no. (%) unless otherwise indicated. Abbreviations: PCP, Pneumocystis jirovecii pneumonia; SD, standard deviation; Q1, first quartile; Q3, third quartile. aMann-Whitney U test; bFisher exact test (for calculation indeterminate values were classified as negative)

Table 2. Test Performance of (1->3)-β-D-glucan for the Diagnosis of *Pneumocystis jirovecii* Pneumonia*

| | Result (95% CI) |
|---|---|
| Sensitivity | 97.5% (87.1%-99.9%) |
| Specificity | 69.01% (60.7%-76.5%) |
| Positive predictive value | 47.6% (41.45%-53.86%) |
| Negative predictive value | 98.9% (93.3%-99.8%) |

*Using > 80 pg/mL as the cutoff for a positive result

***Conclusion.*** At our center where histoplasmosis is endemic, a positive BDG should not be attributed to PCP among PWA with respiratory symptoms because of