Rapid Virologic Suppression With DTG/3TC Facilitates Early Switch to CAB+RPV LA For Treatment-Naive People Living With HIV: Suppression Phase Outcomes From the Phase 3b VOLITION Study

Poster WEPEB033

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Ezequiel Córdova[1], Kai Hove[2], Laurent Hocqueloux[3], Riya Moodley[2], Björn-Erik Ole Jensen[4], Julie Priest[5], Andrea Antinori[6], Parul Patel[5], Guillermo Cuevas Tascón[7], Christopher Polk[5], Marc Johnson[8], Marty St Clair[5], Francisco Xavier Zamora Vargas[9], Suryakant Somvanshi[10], Jason Szabo[11], Jacob Radford[2], Louise Garside[12], Richard Grove[12], Harmony P. Garges[5], Jean van Wyk[2], Bryn Jones[2]

[1]IDEAA Foundation, Buenos Aires, Argentina; [2]ViiV Healthcare, London, United Kingdom; [3]Centre Hospitalier Universitaire d'Orléans, Orléans, France; [4]Department of Gastroenterology, Hepatology, and Infectious Diseases, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University, Düsseldorf, Germany; [5]ViiV Healthcare, Durham, NC, United States; [6]HIV/AIDS Department, National Institute of Infectious Diseases, L. Spallanzani, IRCCS, Rome, Italy; [7]Departamento de Medicina Interna, Hospital Universitario Infanta Leonor, Madrid, Spain; [8]Atrium Health Carolinas Medical Center, Charlotte, NC, United States; [9]Espacio EME, Región Metropolitana, Chile; [10]Development Statistics, GCC, GSK, Bengaluru, India; [11]Clinical Department, L'Actuel Medical Clinic, Montréal, QC, Canada; [12]GSK, London, United Kingdom

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Key Takeaways

- **Once-daily dolutegravir and lamivudine (DTG/3TC) enabled rapid virologic suppression in a diverse population of treatment-naive adults with HIV-1, confirming its high potency and providing a pathway to person-centered treatment, allowing people to choose an early switch to long-acting (LA) therapy of their own VOLITION.**
- **DTG/3TC virologic suppression outcomes were robust across baseline viral load and CD4+ cell count categories.**
- **DTG/3TC was well tolerated and participants maintained high levels of satisfaction throughout the Suppression Phase.**

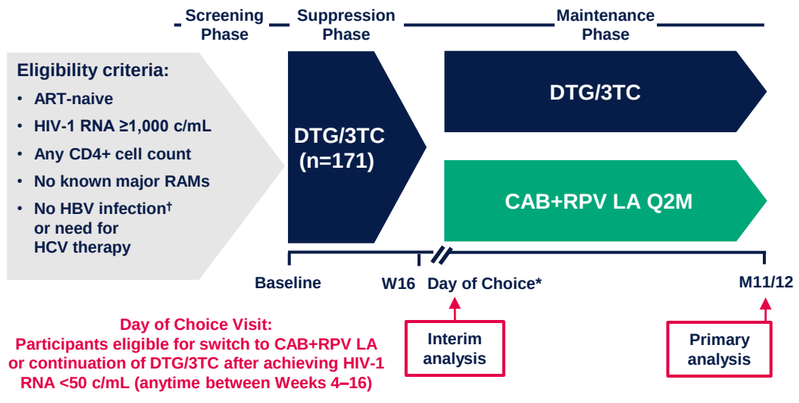
Background

- DTG/3TC has shown rapid and durable virologic suppression, regardless of baseline viral load or CD4+ counts, with rare reports of emergent resistance across numerous clinical trials and real-world studies in both treatment-naive and experienced individuals for over 5 years.[1–5]
- Initial use of DTG/3TC can provide a route for treatment-naive people living with HIV to rapidly achieve virologic suppression and an opportunity to consider early switch to long-acting cabotegravir plus rilpivirine (CAB+RPV LA).
- VOLITION (NCT05917509) is the first study to evaluate optional switch from DTG/3TC to CAB+RPV LA immediately after attaining virologic suppression in antiretroviral therapy-naive adults with HIV-1.
- We present results of the 16-week Suppression Phase during initial treatment with DTG/3TC.

Methods

Figure 1. VOLITION Study Design

Phase 3b, multicenter, non-randomized, parallel-group, open-label, implementation-effectiveness study



*Participants will proceed to Day of Choice at their next study visit following the first plasma HIV-1 RNA result <50 c/mL (Week 4 at the earliest but no later than Week 16). Participants must be suppressed <50 c/mL in order to qualify for option to switch to CAB+RPV LA. Exclusion criteria for switch included: treatment-emergent ALT ≥5×ULN; or ALT ≥3×ULN and bilirubin ≥1.5×ULN (with >35% direct bilirubin) and pregnancy. †Participants positive for HBsAg were excluded. Participants negative for anti-HBs but positive for anti-HBc were excluded only if HBV DNA was detected.
3TC, lamivudine; ALT, alanine aminotransferase; anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; ART, antiretroviral therapy; CAB, cabotegravir; DTG, dolutegravir; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; LA, long-acting; M, month; Q2M, every 2 months; RAM, resistance-associated mutation; RPV, rilpivirine; ULN, upper limit of normal; W, week.

- The VOLITION study evaluated initial viral suppression with DTG/3TC up to ~16 weeks followed by participant-determined optional switch to CAB+RPV LA dosed every 2 months or continuation of DTG/3TC through Month 11/12 (**Figure 1**).
- The co-primary study endpoints were:
  - Time to virologic suppression (HIV-1 RNA <50 c/mL) from baseline.
  - Proportion of participants with HIV-1 RNA <50 c/mL per Snapshot algorithm at Month 11 (CAB+RPV LA).
- Secondary endpoints assessed during the Suppression Phase included:
  - The proportion of participants with HIV-1 RNA <50 c/mL over time.
  - The proportion of participants with confirmed virologic failure (CVF; consecutive plasma HIV-1 RNA values ≥200 c/mL after prior suppression to <50 c/mL) and the development of resistance.
  - Change in CD4+ count over time; safety and tolerability; patient-reported outcomes.
- Virologic non-response was defined as either having a plasma HIV-1 RNA level decrease of <1.0 $\log_{10}$ c/mL by Week 12 or a plasma HIV-1 RNA level of ≥200 c/mL on or after Day of Choice with no history of suppression <50 c/mL and confirmed upon re-test.
- HIV-1 RNA was measured using the Roche cobas 6800 assay for participant management. Prior studies in the DTG/3TC development program have used the Abbott RealTime HIV-1 assay.
- During the study, it was noted in contemporaneous trials that central lab viral load results were inconsistent with local lab findings and clinical assessments, prompting additional testing using the Abbott assay.
- Virologic efficacy analyses presented here are based on Abbott results.

Results

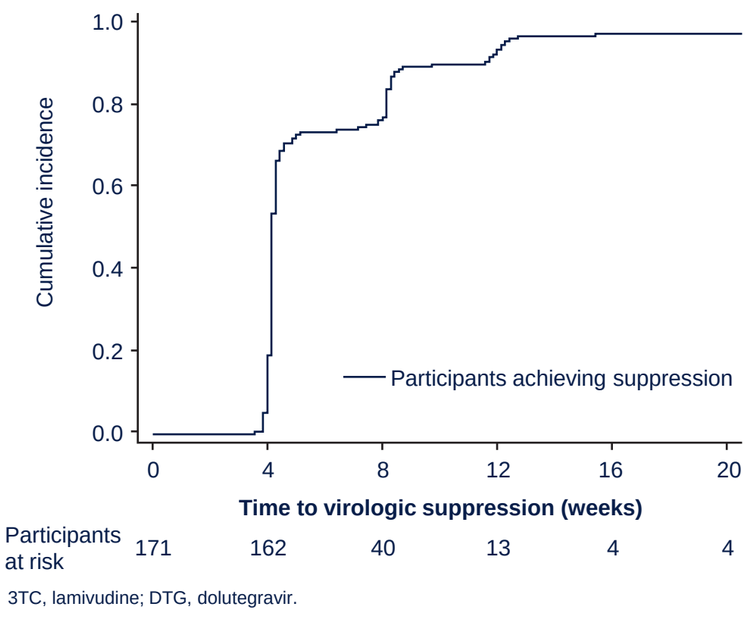
Table 1. VOLITION Enrolled a Diverse Population of Treatment-Naive Adults With HIV-1

Parameter	DTG/3TC (n=171)
Age, years, median (range)	31 (18–70)
≥50 years, n	18 (11)
Women (self-identified gender), n (%)	45 (26)
Race, n (%)	
Black or African American	51 (30)
White	106 (62)
Other races*	7 (4)
Not reported or unknown	7 (4)
Hispanic/Latinx ethnicity, n (%)	88 (51)
Region, n†	
North America	78 (46)
Europe	47 (27)
South America	46 (27)
Plasma HIV-1 RNA, c/mL, median (IQR)	57,100 (21,200, 174,000)
Plasma HIV-1 RNA (c/mL) category, n (%)	
<100,000	106 (62)
100,000 to <500,000	50 (29)
500,000 to <1,000,000	11 (6)
≥1,000,000	4 (2)
CD4+, cells/mm^3, median (IQR)	396 (252, 543)
CD4+ (cells/mm^3) category, n (%)	
<200	27 (16)
200 to <350	46 (27)
≥350	98 (57)
CDC category, n (%)	
Stage 0–2	137 (80)
Stage 3	32 (19)
Stage unknown	2 (1)

*Other race participants: Multiple, n=3; Asian, n=4.
†Argentina (n=28), Canada, (n=9), Chile (n=18), France (n=9), Germany (n=5), Italy (n=16), Spain (n=17), United States (including Puerto Rico; n=69).
3TC, lamivudine; DTG, dolutegravir; IQR, interquartile range.

- A diverse population of 171 participants was enrolled.
  - 26% were female gender, 30% were Black, 51% were Hispanic/Latinx, and 19% had Centers for Disease Control-classified Stage 3 disease (**Table 1**).
  - 9% had a baseline plasma HIV-1 RNA ≥500,000 c/mL and 16% had a baseline CD4+ cell count <200 cells/mm^3.

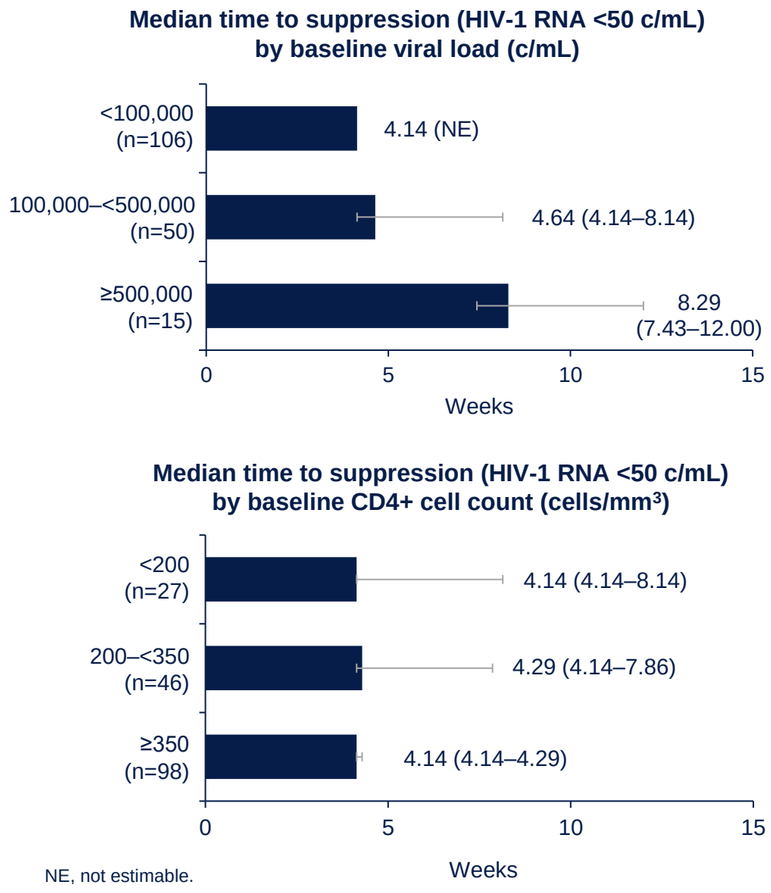
Figure 2. DTG/3TC Enabled Rapid Virologic Suppression (HIV-1 RNA <50 c/mL)



3TC, lamivudine; DTG, dolutegravir.

- Median (95% confidence interval) time to suppression with DTG/3TC was 4.1 (4.1–4.3) weeks and 97.7% (n=167/171) achieved virologic suppression within the 16-week Suppression Phase (**Figure 2**).
- One participant met protocol-defined CVF without treatment-emergent resistance and treatment was not changed.

Figure 3. Virologic Suppression Outcomes Were Robust Across Baseline Viral Load and CD4+ Cell Count Categories



NE, not estimable.

- As expected, median time to suppression was longer in participants with very high baseline viral loads; however, it was similar across CD4+ cell count categories (**Figure 3**).
- High rates of suppression to HIV-1 RNA <50 c/mL were observed during the Suppression Phase regardless of baseline viral load (93–99%) and CD4+ cell count category (96–98%).
- Initial CD4+ cell counts substantially increased from baseline (n=171) to Day of Choice (n=157) with a mean change (standard deviation) of 157.3 cells/mm^3 (216.7).

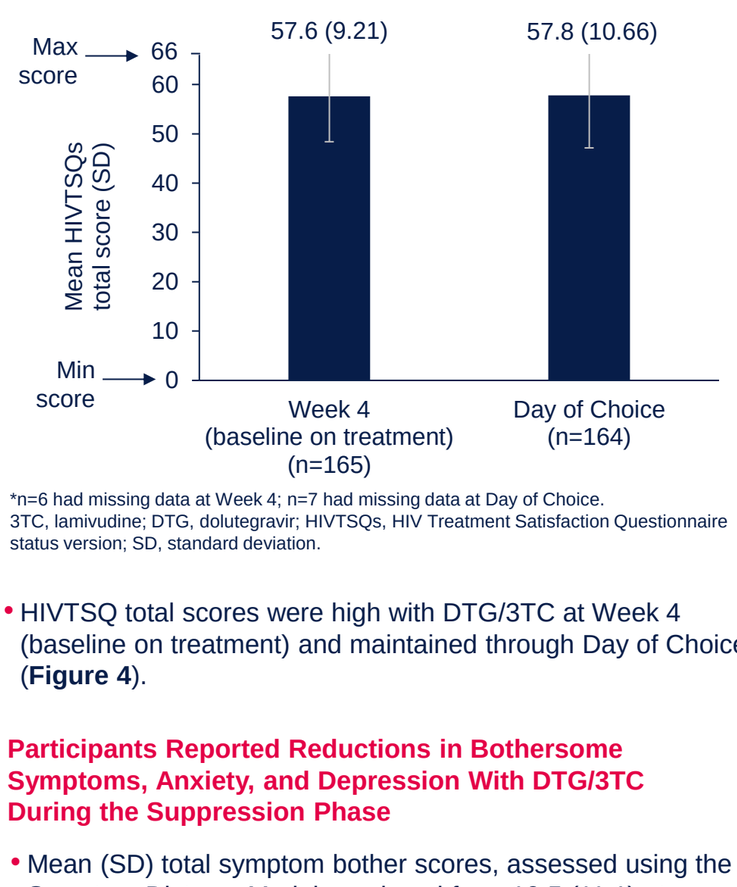
Table 2. DTG/3TC Was Well Tolerated With Few Drug-Related AEs Through the Suppression Phase*

Parameter, n (%)	DTG/3TC (n=171)
Any AE	89 (52)
Any drug-related AEs†	17 (10)
Drug-related AEs reported in ≥2% of participants	
Fatigue	4 (2)
Diarrhea	3 (2)
Dizziness	3 (2)
Any Grade ≥3 AE	10 (6)
Drug-related	0
Any AE leading to withdrawal	1 (<1)‡
Drug-related	0
Any serious AE	5 (3)§
Drug-related	0

*Suppression Phase period was variable for participants. †All were Grade 1 or 2. ‡Pneumocystis jirovecii pneumonia. §Pneumocystis jirovecii pneumonia (n=2); cellulitis (n=1); cytomegalovirus infection reactivation (n=1); lower respiratory tract infection (viral, n=1); cholecystitis (n=1). AE, adverse event; 3TC, lamivudine; DTG, dolutegravir.

- Overall, 10% of participants had a drug-related Grade 1 or 2 adverse event (AE); there were no drug-related Grade ≥3 AEs (**Table 2**).
- No SAEs were considered drug-related and only one (<1%) participant withdrew due to an AE.
- Drug-related AEs were infrequent and consistent with the known safety profile of DTG/3TC.[6]

Figure 4. Treatment Satisfaction With DTG/3TC Was High at Week 4 (Baseline on Treatment) and Day of Choice*



*n=6 had missing data at Week 4; n=7 had missing data at Day of Choice.
3TC, lamivudine; DTG, dolutegravir; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; SD, standard deviation.

- HIVTSQ total scores were high with DTG/3TC at Week 4 (baseline on treatment) and maintained through Day of Choice (**Figure 4**).

Participants Reported Reductions in Bothersome Symptoms, Anxiety, and Depression With DTG/3TC During the Suppression Phase

- Mean (SD) total symptom bother scores, assessed using the Symptom Distress Module, reduced from 10.5 (11.1) at baseline to 7.3 (10.7) at Day of Choice.
  - The top three most frequently reported bothersome symptoms at baseline were nervous/anxious, fatigue/loss of energy, and felt sad/down/depressed; all improved through the Suppression Phase.
- General Anxiety Disorder 7 (GAD-7) and Patient Health Questionnaire 9 (PHQ-9; depression) total mean (SD) scores reduced from baseline (GAD-7, 5.0 [4.4]; PHQ-9, 4.7 [4.7]) to Day of Choice (GAD-7, 3.0 [4.0]; PHQ-9, 3.5 [4.6]).

Participants Reported Positive Opinions About Switching to CAB+RPV LA at Day of Choice

- At baseline, 85% (n=101/119) of participants who had considered what treatment they would choose at Day of Choice expressed an interest in switching to CAB+RPV LA therapy.
- Positive opinion for switching to CAB+RPV LA was maintained from baseline to Day of Choice, with 89% (n=129/145) of eligible participants choosing to switch to CAB+RPV LA (see Poster EP0170 for further details on participants' perceptions of switching).[7]

Conclusions

- Once-daily DTG/3TC enabled rapid virologic suppression in a diverse population of treatment-naive adults with HIV-1, confirming its high potency and providing a pathway to person-centered treatment, allowing people to choose an early switch to LA therapy of their own VOLITION.
  - A total of 98% of participants achieved virologic suppression on DTG/3TC by Day of Choice.
  - The median time to virologic suppression on DTG/3TC was 4 weeks.
- Rates of suppression with DTG/3TC were high regardless of baseline viral load or CD4+ count category.
- Initial CD4+ cell count recovery increased rapidly with DTG/3TC from baseline to Day of Choice.
- DTG/3TC was well tolerated with no new safety signals identified. Participants reported high levels of treatment satisfaction as well as reductions in bothersome symptoms, anxiety, and depression during the Suppression Phase.
- Most participants expressed an interest in switching to CAB+RPV LA at baseline and the majority of those who were eligible chose to switch at Day of Choice.

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Presenting author: Bryn Jones; bryn.c.jones@viivhealthcare.com

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