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MAJOR ARTICLE

Proof-of-Concept Phase 2a Trial of VH4524184 (VH-184), an Emerging Third-Generation Integrase Strand Transfer Inhibitor With an Enhanced Resistance Profile

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Background: VH4524184 (VH-184) is an emerging third-generation integrase strand transfer inhibitor (INSTI) with an enhanced in vitro resistance profile compared with second-generation INSTIs being developed as a long-acting antiretroviral therapy (ART) for HIV-1. We present data from a proof-of-concept phase 2a trial of VH-184 in people with HIV-1.

Methods: This randomized, double-blind, placebo-controlled trial evaluated oral VH-184 monotherapy in adults naive to ART with HIV-1 RNA ≥3000 copies/mL. Participants received

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oral VH-184 10, 50, or 300 mg or placebo on Days 1 (baseline), 4, and 7. On Day 10, participants initiated standard-of-care ART. The primary endpoint was maximum change from baseline in plasma HIV-1 RNA through Day 10. Secondary endpoints included safety, tolerability, exposure-response relationship, CD4+ cell effects, and treatment-emergent resistance.

Results: Of 22 participants enrolled (VH-184, n=19; placebo, n=3), 86% were male, 68% were White, and median age was 32 years. Mean maximum change from baseline through Day 10 in HIV-1 RNA was −1.17, −2.15, and −2.31 $\log_{10}$ copies/mL for VH-184 10, 50, and 300 mg, respectively. No adverse events (AEs) leading to withdrawal, treatment-emergent serious AEs, or deaths occurred. There were no clinically relevant changes in safety laboratory parameters, electrocardiograms, or vital signs. No VH-184 genotypic or phenotypic resistance was detected through Day 10.

Conclusions: VH-184 monotherapy demonstrated rapid and potent antiviral activity and a favorable safety and tolerability profile. The established exposure-response model and efficacy and safety results support further development of VH-184 as the core agent in complete ART regimens for HIV-1 (ClinicalTrials.gov, NCT06214052).

Keywords: HIV-1; long-acting antiretroviral therapy; pharmacokinetics; safety; treatment naive

Key points: In this proof-of-concept phase 2a study, monotherapy with VH4524184, a third-generation integrase strand transfer inhibitor with an enhanced resistance profile, demonstrated rapid and highly potent antiviral activity and a favorable safety and tolerability profile in adults naive to antiretroviral therapy.

INTRODUCTION

Advances in antiretroviral therapy (ART) have improved the life expectancy of people with HIV, and with successful treatment, it is now comparable to that of the general population [1, 2]. However, daily oral ART is associated with challenges such as unwanted reminders of HIV, unintended sharing of HIV status, pill fatigue, and stigma of being seen taking medication [3]. Long-acting ART is a promising treatment strategy that addresses these challenges and is likely to become the standard of care (SOC). Advancing long-acting ART is imperative to provide people with HIV with more convenient and sustainable choices, enhancing quality of life and adherence, while paving the way to end the epidemic [3, 4].

Second-generation integrase strand transfer inhibitors (INSTIs) are widely recommended as initial therapy for most people with HIV-1 due to their strong efficacy and high barrier to resistance [5]. However, their widespread use necessitates development of newer INSTIs with even higher barriers to resistance [6]. Additionally, new INSTIs with long-acting potential are needed to expand treatment options and address the unmet needs of people with HIV [7].

VH4524184 (VH-184) is an emerging third-generation INSTI based upon its enhanced in vitro resistance profile compared with second-generation INSTIs, combined with long-acting potential and potent in vitro antiviral activity comparable to the second-generation INSTIs dolutegravir (DTG), cabotegravir (CAB), and bictegravir [7-9]. In vitro passage experiments showed VH-184 has a high barrier to resistance that is higher than or equivalent to that of second-generation INSTIs, and VH-184 retained antiviral activity against second-generation INSTI-resistant viruses, including those with multiple INSTI resistance-associated mutations (RAMs) [8]. VH-184 also retained antiviral activity against second-generation INSTI-resistant pseudotyped viruses containing participant-derived sequences from the phase 3 SAILING and DAWNING studies [7].

Orally administered VH-184 demonstrated a good safety and tolerability profile in adults without HIV in a phase 1 first-time-in-human (FTIH) study, and VH-184 elimination half-life was approximately 24 hours [7]. Together, the enhanced in vitro resistance profile, good safety and tolerability profile, and pharmacokinetic (PK) properties of VH-184 support its further development as an emerging third-generation INSTI with long-acting potential for HIV-1 treatment.

Here, we present antiviral activity, PK, safety, and tolerability data for oral VH-184 from a proof-of-concept phase 2a trial in people with HIV-1 naive to ART.

METHODS

Study design

We conducted this randomized, double-blind, placebo-controlled trial to evaluate oral VH-184 monotherapy in adults naive to ART at 14 centers in Argentina, Canada, Italy, Spain, and the United States (ClinicalTrials.gov, NCT06214052; Figure 1). After a 7- to 14-day screening period (maximum of 28 days allowed), we randomized participants to 1 of 3 cohorts, with at least n=6 receiving oral VH-184 and n=1 receiving matching oral placebo in each cohort. During the 10-day monotherapy period, participants received oral VH-184 10, 50, or 300 mg or matching placebo on Days 1 (baseline), 4, and 7. On Day 10, participants started open-label, locally sourced, SOC combination ART and were followed weekly through Day 38 (follow-up period). Participant visits took place from February 7, 2024, to June 12, 2024, with a database lock date of July 26, 2024.

We conducted this study in accordance with legal and regulatory requirements and the principles in the Declaration of Helsinki. Institutional reviews boards and independent ethics committees (listed in Supplementary Table 1) reviewed and approved the study protocol and other relevant documents, and all participants provided written informed consent before study enrollment.

Participants

This study included people with HIV-1 naive to ART who were aged 18 to 65 years and had confirmed HIV-1 RNA ≥3000 copies/mL and CD4+ cell count ≥200 cells/mm^3 at screening. Eligible participants also had a body mass index of 18.5 to 31.0 kg/m^2 and no prior use of any INSTI for HIV-1 pre-exposure or post-exposure prophylaxis. Key exclusion criteria included primary HIV infection, evidence of active Centers for Disease Control and Prevention stage 3 disease, untreated syphilis, ongoing malignancy, use of immunomodulating agents or any agent with known anti-HIV activity, receipt of an investigational HIV vaccine, or presence of hepatitis B core antibody or surface antigen at screening.

Assessments

The primary endpoint was maximum change from baseline in plasma HIV-1 RNA through Day 10. Secondary endpoints included safety, tolerability, exposure-response relationship, CD4+ cell effects, and treatment-emergent resistance.

Assessments were performed at 5 in-clinic visits (Days 1, 2, 4, 7, and 10) and 3 virtual visits (Days 3, 5 or 6, and 8 or 9; participants could choose to have these visits in-clinic) during the monotherapy period and 4 in-clinic visits (Days 17, 24, 31, and 38) during the open-label follow-up period. Blood draws for HIV-1 RNA measurement and PK sampling were performed on Days 1, 2, 4, 7, and 10 during the monotherapy period, and a blood draw for HIV-1 RNA was taken at the Day 38 visit during the follow-up period. Intensive PK sampling occurred on Days 1 and 7, with samples collected pre-dose and 0.5, 1, 2, 4, 5, 6, 7, 8, and 12 hours post-dose. Plasma samples from Day 1 (baseline) and Day 10 were batch-tested for viral genotypic and phenotypic on-treatment changes or INSTI resistance using assays from Monogram Biosciences (South San Francisco, CA).

Safety was assessed using incidence of adverse events (AEs), severity of AEs, and proportion of participants who discontinued study treatment due to AEs. The Division of AIDS grading tables (version 2.1, July 2017) were used to grade the severity of each reported AE [10]. Change from baseline in liver laboratory parameters was also assessed. Twelve-lead electrocardiograms were obtained at the Day 1 and Day 38 visits, and vital signs were measured on Days 1, 2, 4, 7, and 10 during the monotherapy period and at each visit during the follow-up period.

To ensure consistency across the study sites, all efficacy and safety assessments were processed via a central laboratory, and standardized training was required for all qualified study personnel.

Statistical and exposure-response analysis

The primary endpoint was assessed using descriptive statistics with no hypothesis testing. For all endpoints, the baseline value was the latest pre-dose assessment with a non-missing value,

including those from unscheduled visits. The primary treatment effect was estimated using maximum change from baseline in plasma HIV-1 RNA over the

monotherapy period. To derive PK parameters, plasma concentration–time data were analyzed using non-compartmental methods with WinNonlin™ software (version 8.3; Certara, Radnor, PA). The exposure-response relationship between steady-state PK parameters maximum plasma concentration (Cmax), minimum plasma concentration (Cmin), plasma concentration at the end of the dosing interval (C_τ), area under the plasma concentration–time curve from time 0 to the end of the dosing interval ($AUC_{0-\tau}$), and maximum change from baseline in $\log_{10}$ plasma HIV-1 RNA were explored with simple and sigmoidal maximum effect (Emax) models. Models were evaluated using Akaike information criteria and goodness-of-fit plots. For the primary endpoint, safety, and PK analyses, missing data were not imputed.

RESULTS

Demographics and baseline characteristics

Of 32 individuals screened, 22 were enrolled and randomized in the study (Table 1), with Spain contributing the highest overall enrollment. All 22 participants received the expected number of VH-184 or placebo doses and completed the study. The majority of participants were male (86% [19/22]), 68% (15/22) were White, and 59% (13/22) were of Hispanic or Latin American ethnicity, with a median (range) age of 32 (19-60) years.

Efficacy

During the monotherapy period, plasma HIV-1 RNA decreased in all VH-184 treatment groups, with the largest changes from baseline to Day 10 occurring with 300 and 50 mg (Figure 2). Mean maximum change from baseline in plasma HIV-1 RNA was −1.17, −2.15, and −2.31 $\log_{10}$ copies/mL for VH-184 at doses of 10, 50, and 300 mg, respectively. Changes to plasma HIV-1 RNA in the placebo group were minimal.

At baseline, mean CD4+ cell counts were 387 (204), 596 (330), and 491 (276) cells/mm^3 in the VH-184 10, 50, and 300 mg groups, respectively, and 661 (200) cells/mm^3 in the placebo group. From baseline to Day 10, mean (SD) CD4+ cell count increased by 131 (98), 69 (122), and 47 (46) cells/mm^3 in the VH-184 10, 50, and 300 mg groups, respectively, which was comparable to the increase of 64 (216) cells/mm^3 observed in the placebo group. Mean (SD) CD4+ cell/lymphocyte percentages at baseline were 28% (8%), 31% (12%), and 27% (6%) in the VH-184 10, 50, and 300 mg groups, respectively, and 33% (8%) in the placebo group. From baseline to Day 10, mean (SD) CD4+ cell/lymphocyte percentages increased by 1% (3%), 0% (3%), and 2% (4%) in the VH-184 10, 50, and 300 mg groups, respectively. No increase in CD4+ cell/lymphocyte percentage was observed in the placebo group (mean [SD], 0% [6%]). Mean (SD) CD4+/CD8+ ratio increased from baseline to Day 10 by 0.50 (0.11), 0.02 (0.07), and 0.10 (0.13) in the VH-184 10, 50, and 300

mg groups, respectively, which was similar to the increase of 0.02 (0.14) observed in the placebo group.

No genotypic or phenotypic resistance to VH-184 was detected at the end of the monotherapy period (Day 10) in participants with available data. VH-184 half-maximal inhibitory concentration (IC_{50}) range for Day 1 was 2.01 to 8.47 nM, and the range of fold-change in IC_{50} from Day 10 to Day 1 was 0.58 to 1.45, although assays on Day 10 samples failed for 9 participants with low viral loads (n=1 in the 10 mg group and n=4 each in the 50 and 300 mg groups). The HIV-1 integrase genotype was successfully obtained and compared between Days 1 and 10 in 16 participants. At Day 1 (prior to dosing), 4 participants had L47 polymorphisms: 2 in the VH-184 10 mg group (L47I and L74L/M) and 1 each in the 50 mg and 300 mg groups (each with L74I). No emergent INSTI RAMs were detected among participants with available data.

Pharmacokinetics and exposure-response analysis

VH-184 was rapidly absorbed with no apparent lag time after both single and repeat dose administration (Table 2). Dose proportionality was assessed by pairwise comparisons of Day 7 dose-normalized AUC over an interval with interpolation or extrapolation (AUC_{INT}) using an analysis of variance model. VH-184 exposures increased dose proportionally from 10 to 50 mg (AUC_{INT} ratio, 0.932; 90% CI, 0.699-1.243) and less than dose proportionally from 10 to 300 mg (AUC_{INT} ratio, 0.448; 90% CI, 0.339-0.591; Supplementary Table 2; Supplementary Figure 1). Maximum concentrations were achieved within approximately 2 to 4.5 hours across dose levels, with an elimination half-life ranging from approximately 19 to 22.5 hours.

A strong relationship was observed between steady-state (Day 7/10) VH-184 PK parameters and HIV-1 RNA reduction from baseline to Day 10. Among the various models used to evaluate the relationship between reduction in plasma HIV-1 RNA from baseline to Day 10 and steady-state PK parameters (Day 7/10), the oral VH-184 exposure-antiviral relationship was best described with a simple Emax model (Hill coefficient = 1; E0 = 0). Among all PK parameters showing exposure-response relationships, Cmin was selected on the basis of its relevance to the development of long-acting injectable formulations (Figure 3). Using the Cmin exposure metric, the estimated Emax maximum HIV-1 RNA decline after 10 days of VH-184 monotherapy was −2.54 log_{10} copies/mL and the EC_{50} was 0.099 µg/mL.

Safety

During the monotherapy period, 42% (8/19) of participants receiving VH-184 and 67% (2/3) receiving matching placebo experienced AEs (Table 3). We observed no trends in types of AEs reported across treatment groups. Vomiting was the only AE reported in >1 participant (n=1 each in the VH-184 50 and 300 mg groups). Both AEs of vomiting were mild in severity; 1 was considered drug-related in the VH-184 300 mg group and the other was considered unrelated in the VH-184 50 mg group. Both events resolved within 1 day, and neither of these AEs impacted dosing. Drug-related AEs were reported in 26% (5/19) of participants receiving VH-184, with n=1

event each of diarrhea, dizziness, fatigue, increased amylase, increased lipase, nausea, and vomiting. All drug-related AEs were grade 1. No AEs with an onset during the follow-up period were considered related to study drug. No deaths or treatment-emergent serious AEs were reported during the study, and no AEs resulted in study drug discontinuation or study withdrawal.

No clinically relevant changes were observed in leukocyte, lymphocyte, and neutrophil counts or lymphocyte/leukocyte percentage during the monotherapy period (Supplementary Tables 3 and 4). No clinically relevant changes were observed across treatment groups in laboratory parameters (Supplementary Tables 5 and 6), electrocardiograms, or vital signs during the monotherapy or follow-up periods.

DISCUSSION

In this proof-of-concept study, VH-184, an emerging third-generation INSTI, demonstrated rapid and highly potent antiviral activity in people with HIV-1. The decreases in HIV-1 RNA that we observed with VH-184 (mean maximum change from baseline −1.17 to −2.31 $\log_{10}$ copies/mL) were comparable to those seen with DTG during monotherapy (−1.51 to −2.46 $\log_{10}$ copies/mL) [11]. No INSTI-resistant mutations were selected, although genotypic resistance testing failed to produce results in 6/22 participants at Day 10.

Modest and variable increases in mean CD4+ cell count and CD4+/CD8+ ratio were observed across the VH-184 and placebo groups. Increases in CD4+ cell counts with VH-184 through Day 10 were generally comparable to those observed with DTG and CAB monotherapy [11, 12]. Notably, the mean increases in CD4+ cell count in the VH-184 50 and 300 mg groups (69 and 47 cells/mm^3, respectively) were similar to the median increase observed with DTG 50 mg monotherapy at Day 11 (64 cells/mm^3) [13]. This dose of DTG has consistently shown robust and durable increases in CD4+ cell count in people naive to ART when used as part of a complete regimen [14, 15]. There were no safety signals regarding immune parameters.

VH-184 PK parameters in participants naive to ART were similar to those in participants without HIV from the oral FTIH study [7]. VH-184 PK parameters increased dose proportionally from 10 to 50 mg and less than dose proportionally from 10 to 300 mg. Lack of dose proportionality may be due to solubility-limited oral saturation or differences in bioavailability of 10 and 100 mg tablets.

We observed minimal accumulation of VH-184 after repeat oral administration. VH-184 was rapidly absorbed, with no apparent lag time after single or repeat dose administration. The estimated maximum HIV-1 RNA decline after 10 days of VH-184 monotherapy was −2.69 $\log_{10}$ copies/mL, similar to DTG monotherapy (−2.6 $\log_{10}$ copies/mL) [11]. Using the Cmin exposure metric, which is more relevant for long-acting treatment development, Emax and EC_{50} were

estimated at −2.54 $\log_{10}$ copies/mL and 0.099 µg/mL, respectively. These findings provide support for the long-acting potential of VH-184.

VH-184 was also well tolerated and had a favorable safety profile. There were no noteworthy differences between treatment groups in incidence of AEs during the 10-day monotherapy period, and there were no treatment-emergent serious AEs, AEs leading to withdrawal, or deaths reported during the study. We also observed a favorable safety and tolerability profile in the phase 1 FTIH study of VH-184 [7].

Strengths of this study include a racially and ethnically diverse study population facilitated by a multi-national and multi-site enrollment strategy, which allowed timely enrollment of people with HIV-1 naive to ART. Additionally, all participants completed the study. Limitations include the small overall sample size, with only 3 (14%) female participants, limiting generalizability. The sex imbalance can be addressed by inclusion of greater proportions of female participants in future trials. Although the use of 14 clinical sites introduced logistical complexity, the centralized laboratory assessments reduced site-specific bias. Protocol deviations were observed involving out-of-window assessments/PK sample collection (n=7 participants) and procedural errors with biologic specimen sampling or equipment (n=5 participants). Importantly, no protocol deviations impacted the integrity of the analyses.

In this proof-of-concept study, we established the rapid and highly potent antiviral activity as well as the favorable safety and tolerability profile of VH-184 monotherapy in adults with HIV-1. These findings, in combination with FTIH study results and the enhanced in vitro resistance profile of VH-184 vs second-generation INSTIs [7-9], support further development of VH-184 as the core agent in new ART regimens designed to address unmet needs. We are currently evaluating long-acting injectable formulations of VH-184 in adults without HIV in an ongoing phase 1 study (NCT06310551).

NOTES

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interpretation of data. LR, ML, NH, GLG, JRC-M, FH, and EE contributed to drafting the manuscript. All authors contributed to critically revising the manuscript for important intellectual content and approve the manuscript for publication.

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Potential conflicts of interest: LR, ML, NH, GLG, JLJ, MU, JRC-M, FH, EE, and MG are employees of ViiV Healthcare or GSK and may own stock in GSK. SAN has received grants/contracts and travel/meeting support from GSK. MVM has served as a principal investigator for and received travel/meeting support from ViiV Healthcare/GSK. PD has received consulting fees and honoraria from Gilead, Janssen-Cilag, MSD, and ViiV Healthcare. C-PR has participated in speakers bureaus for Gilead and ViiV Healthcare, served as an advisor to ViiV Healthcare, and received research grants (paid to institution) from Gilead, MSD, and ViiV Healthcare. RG-F has received grants, consulting fees, honoraria, and travel/meeting support from Gilead and ViiV Healthcare. VE has received travel/meeting support from Gilead and Johnson & Johnson and participated on data safety monitoring/advisory boards for Johnson & Johnson and ViiV Healthcare.

Data availability statement: Anonymized individual participant data and study documents can be requested for further research from www.clinicalstudydatarequest.com.

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ALT TEXT

Figure 1. Study design diagram displaying the randomized treatment groups, dosing schedule, and study periods.

Figure 2. Graph depicting the mean maximum decreases in plasma HIV-1 RNA from baseline during the VH4524184 monotherapy period.

Figure 3. Graph depicting the exposure-response relationship of the maximum observed VH4524184 plasma concentration and plasma HIV-1 RNA reduction in a maximum effect model.

TABLES

Table 1. Participant Demographics and Baseline Characteristics (Safety Population)

Parameter	VH-184 10 mg Q3D (N=6)	VH-184 50 mg Q3D (N=6)	VH-184 300 mg Q3D (N=7)	Placebo Q3D (N=3)	Total (N=22)
Age, median (range), y	34 (21-51)	33 (19-59)	31 (23-60)	31 (25-32)	32 (19-60)
Male, n (%)[a]	6 (100)	4 (67)	6 (86)	3 (100)	19 (86)
Race, n (%)					
American Indian or Alaska Native	1 (17)	0	2 (29)	0	3 (14)
Asian	0	1 (17)	0	0	1 (5)
Black or African American	1 (17)	0	0	2 (67)	3 (14)
White	4 (67)	5 (83)	5 (71)	1 (33)	15 (68)
Ethnicity, Hispanic or Latin American, n (%)	3 (50)	2 (33)	7 (100)	1 (33)	13 (59)
Body mass index, mean (SD), kg/m^2	23.9 (2.5)	23.0 (2.1)	23.6 (2.7)	24.1 (3.1)	23.6 (2.4)
Baseline CD4+ cell count, mean (SD), cells/mm^3	387 (204)	596 (330)	491 (276)	661 (200)	NA
Baseline plasma HIV-1 RNA, mean (SD), log_{10} copies/mL	5.00 (0.79)	4.74 (0.73)	4.32 (0.67)	4.42 (0.93)	NA

NA, not available; Q3D, every 3 days; VH-184, VH4524184. [a]Sex assigned at birth.

Table 2. Plasma VH-184 PK Parameters After Oral Administration of Single and Repeat Doses (PK Population)

Parameter[a]	VH-184 10 mg Q3D (N=6)	VH-184 50 mg Q3D (N=6)	VH-184 300 mg Q3D (N=7)
Day 1			
$AUC_{0\text{-}72h}$, h·µg/mL	29.0 (27.4)	123.4 (22.5)	492.7 (41.7)
Cmax, µg/mL	1.3 (16.8)	6.2 (30.7)	23.6 (32.4)
C_{72}, µg/mL	0.1 (80.7)	0.4 (39.8)	1.5 (52.8)
tmax, h[b]	3.1 (1.0-5.0)	4.0 (2.0-5.0)	2.0 (1.0-5.0)
Day 7			
$AUC_{0\text{-}72h}$, h·µg/mL	34.1 (27.5)	158.9 (28.5)	457.8 (30.9)
Cmax, µg/mL	1.5 (32.1)	7.1 (16.6)	23.1 (45.8)
Cmin, µg/mL	0.1 (66.1)	0.5 (59.7)	2.9 (184.1)
C_T, µg/mL	0.1 (62.5)	0.5 (59.0)	1.2 (42.2)
tmax, h[b]	4.0 (0.5-5.1)	4.5 (1.0-6.0)	2.1 (1.0-4.0)

$AUC_{0\text{-}72h}$, area under the plasma concentration–time curve from time 0 to 72 hours; C_{72}, observed plasma concentration at 72 hours; Cmax, maximum observed plasma concentration; Cmin, minimum observed plasma concentration; C_T, observed plasma concentration at the end of the dosing interval; %CVb, percentage between-participant coefficient of variation; PK, pharmacokinetics; Q3D, every 3 days; tmax, time to Cmax; VH-184, VH4524184.

[a]Values are geometric mean (%CVb) unless otherwise noted. [b]Values are median (range).

Table 3. Participants Reporting AEs During the Monotherapy Period (Safety Population)

Parameter, n (%)	VH-184 10 mg Q3D (N=6)	VH-184 50 mg Q3D (N=6)	VH-184 300 mg Q3D (N=7)	Total VH-184 Q3D (N=19)	Placebo Q3D (N=3)
Any AE	2 (33)	3 (50)	3 (43)	8 (42)	2 (67)
Grade 1	2 (33)	3 (50)	2 (29)	7 (37)	2 (67)
Grade 2	0	0	1 (14)[a]	1 (5)	0
Grade 3-5	0	0	0	0	0

AEs reported in >1 participant					
Vomiting	0	1 (17)	1 (14)	2 (11)	0
Drug-related AEs[b]	1 (17)	2 (33)	2 (29)	5 (26)	0

AE, adverse event; Q3D, every 3 days; VH-184, VH4524184. [a]Non–drug-related AE of influenza-like illness was reported as grade 2 in the monotherapy period, improved to grade 1 during the follow-up period, and resolved 9 days after initial onset. [b]All drug-related AEs were grade 1 (n=1 event each of diarrhea, dizziness, fatigue, increased amylase, increased lipase, nausea, and vomiting).

FIGURE LEGENDS

Figure 1. Proof-of-concept phase 2a study design. cART, combination antiretroviral therapy; PA-IC_{90}, protein-adjusted 90% inhibitory concentration; Q3D, every 3 days; SOC, standard of care; VH-184, VH4524184. [a]Target concentration of 1 × PA-IC_{90}. [b]Target concentration of 4 × PA-IC_{90}. [c]Target concentration of 24 × PA-IC_{90}. [d]Participants received oral VH-184 or matching placebo on Days 1 (baseline), 4, and 7.

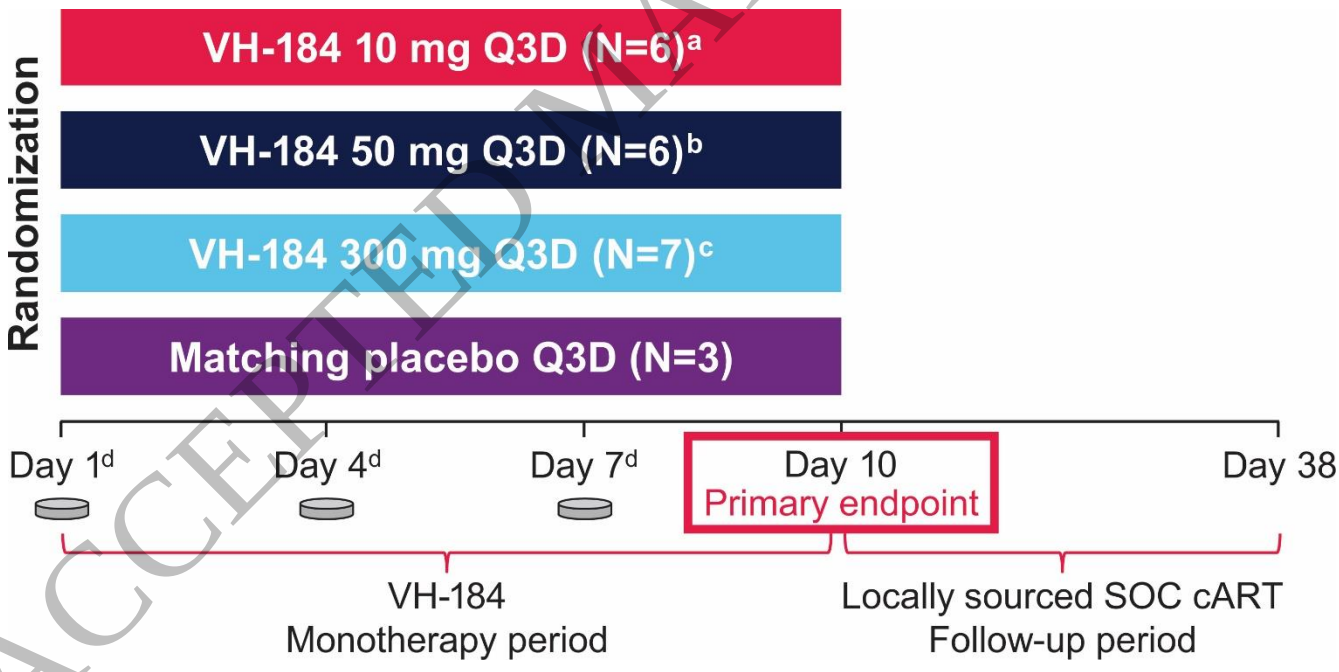

Figure 2. Mean maximum change from baseline in plasma HIV-1 RNA during the monotherapy period (full analysis set). cART, combination antiretroviral therapy; Q3D, every 3 days; SOC, standard of care; VH-184, VH4524184.

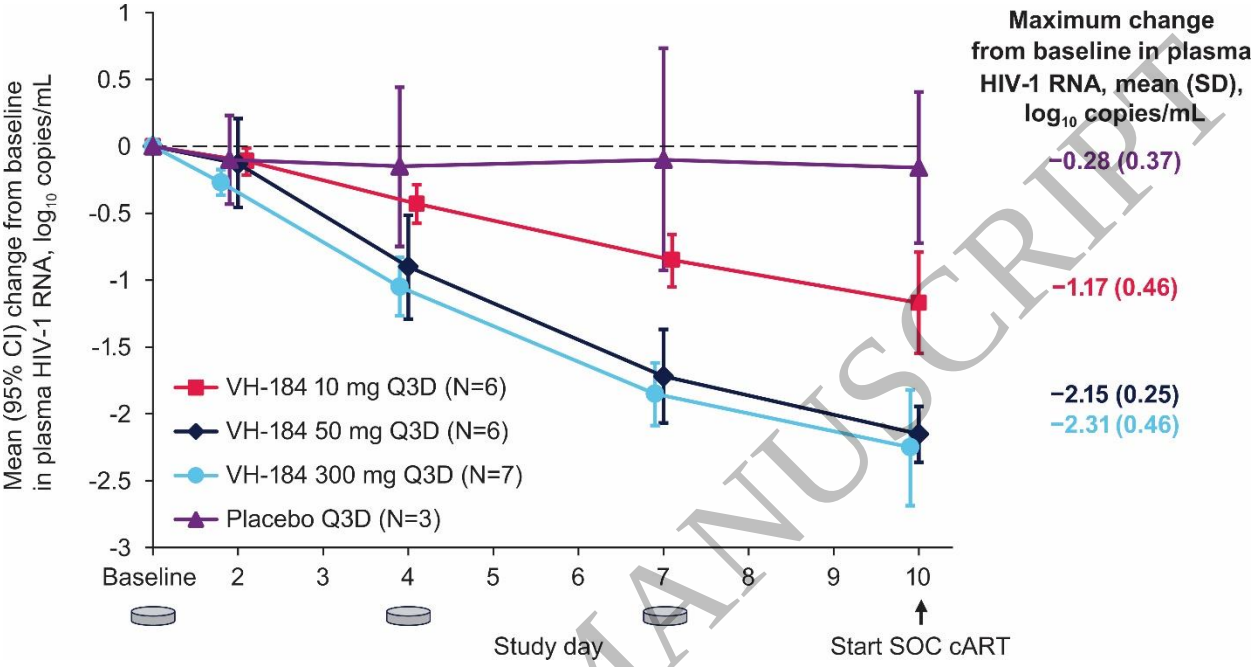

Figure 3. Emax model of the VH-184 exposure-response relationship. Cmin, minimum observed plasma concentration; Emax, maximum effect; Q3D, every 3 days; VH-184, VH4524184. [a]1 participant receiving VH-184 300 mg had screening HIV-1 RNA ≥3000 copies/mL but a baseline HIV-1 RNA value of 838 copies/mL and was excluded from the Emax modeling analysis.