Similar Efficacy, Safety and CD4 T-cell Increase up to Week 96 Observed With Fostemsavir (FTR)-Based Regimens in the BRIGHTE Study and Dolutegravir (DTG)-Based Regimens in the VIKING-3 Study in Individuals With Multidrug-Resistant (MDR) HIV-1

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Antonella Castagna,[1] Natalia Gregori,[2] Iacopo Marcon,[2] Fangfang Du,[3] Bo Li,[3] Marcia Wang,[3] Alftan Dyson,[4] Bryn Jones,[5] Manyu Prakash,[5] Andrew Clark[5]

[1]Vita-Salute San Raffaele University and IRCCS San Raffaele Scientific Institute, Milan, Italy; [2]ViiV Healthcare, Verona, Italy; [3]GSK, Collegeville, PA, USA; [4]ViiV Healthcare, Durham, NC, USA; [5]ViiV Healthcare, London, UK

Key Takeaways

- The phase 3 BRIGHTE and VIKING-3 studies evaluated fostemsavir (FTR)- and dolutegravir (DTG; twice daily [BID])-based regimens, respectively, in people living with multidrug-resistant (MDR) HIV-1 and limited antiretroviral (ARV) options
- Through 96 weeks, FTR- and DTG (BID)-based regimens demonstrated robust virologic suppression and promoted immune recovery in this population
- These results provide additional support that effective ARV regimens can be constructed for individuals living with MDR HIV-1

Introduction

- Constructing suppressive ARV regimens in individuals living with MDR HIV-1 can be challenging, but its success is essential to enable preservation of future treatment options, reduce risk of opportunistic infections, and improve overall survival[1,2]
- The virologic, immunologic, and safety outcomes for people living with MDR HIV-1 and limited ARV options were assessed separately from the phase 3 BRIGHTE and VIKING-3 studies at Week 96

Methods

BRIGHTE Study Design[3]

- BRIGHTE included adults (aged ≥18 years) living with MDR HIV-1 who were heavily treatment-experienced and on a failing ARV regimen with HIV-1 RNA ≥400 c/mL and ≤2 fully active and available ARV classes remaining
- Participants with 1 to 2 fully active ARVs remaining were randomly assigned 3:1 to receive FTR 600 mg BID or placebo + current failing regimen (Randomized Cohort) for 8 days followed by open-label FTR + optimized background therapy (OBT) for all participants up to Week 240
  - BRIGHTE remains ongoing until all participants can access FTR by other means

VIKING-3 Study Design[4]

- VIKING-3 included adults (aged ≥18 years) living with MDR HIV-1 who were heavily treatment-experienced and on a failing ARV regimen containing raltegravir or elvitegravir with HIV-1 RNA ≥500 c/mL and ≥1 fully active ARV for OBT
- Participants received DTG 50 mg BID to replace raltegravir or elvitegravir in their previous failing regimen for 7 days (functional monotherapy period) followed by DTG 50 mg BID + OBT from Day 8 up to Week 180

Results

Participant Demographics and Baseline Characteristics

Table 1. Demographics and Baseline Characteristics: BRIGHTE Randomized Cohort

Characteristic	Randomized Cohort (N=272)
Age, median (range), y	48 (18-73)
Male sex at birth, n (%)	200 (74)
White race, n (%)	185 (68)
HIV-1 RNA, median (range), $\log_{10}$ c/mL	4.66 (1.59-6.91)
CD4+ T-cell count, median (range), cells/mm^3	100 (0-1160)
CD4+/CD8+ ratio, median (range)	0.14 (0.0-1.9)
History of AIDS, n (%)	231 (85)
>20 y of prior ART experience, n (%)	92 (34)
Baseline genotypic integrase resistance detected, n (%)	118 (43)
Most common ARV in initial OBT, n (%)	
DTG[a]	229 (84)
DRV	134 (49)

[a]171/272 (63%) used DTG BID.

Table 2. Demographics and Baseline Characteristics: VIKING-3

Characteristic	DTG 50 mg BID (N=183)
Age, median (range), y	48 (19-67)
Male sex at birth, n (%)	141 (77)
White race, n (%)	130 (71)
HIV-1 RNA, median (range), $\log_{10}$ c/mL	4.38 (1.59-7.37)
CD4+ T-cell count, median (range), cells/mm^3	140 (19-1100)
CD4+/CD8+ ratio, median (range)	0.15 (0.0-1.1)
CDC classification C: AIDS, n (%)	102 (56)
Duration of prior ART, median (range), y	14 (<1-27)
Baseline genotypic primary integrase resistance detected, n (%)	123 (67)
Most common ARV in initial OBT, n (%)[4]	
DRV/r	119 (65)
TDF/FTC	109 (60)

CDC, Centers for Disease Control and Prevention.

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References: 1. Galli et al. *Open Forum Infect Dis*. 2020;7:ofaa456. **2.** Temereanca and Ruta. *Front Microbiol*. 2023;14:1133407. **3.** Lataillade et al. *Lancet HIV*. 2020;7:e740-e751. **4.** Castagna et al. *J Infect Dis*. 2014;210:354-362.

BRIGHTE Randomized Cohort Virologic Outcomes

- In the intention-to-treat–exposed population (Randomized Cohort), 60% (163/272) had HIV-1 RNA <40 c/mL (Snapshot) at Week 96
- By observed analysis, the proportion of participants with virologic response generally increased over time (Figure 1)

BRIGHTE Randomized Cohort Immunologic Outcomes

- Improvements in CD4+ T-cell count (Figure 2) and CD4+/CD8+ ratio (Figure 3) were observed through Week 96

BRIGHTE Randomized Cohort Safety

- Adverse events (AEs) were reported in 92% (249/272) of participants
- Through Week 96, serious AEs were reported in 34% (92/272) of participants; 3% (9/272) were drug-related
  - Serious AEs were most commonly reported from the infections and infestations system organ class
- AEs leading to discontinuation were reported in 5% (14/272) of participants

Figure 1. Virologic Response Through Week 96 by Observed Analysis: BRIGHTE Randomized Cohort

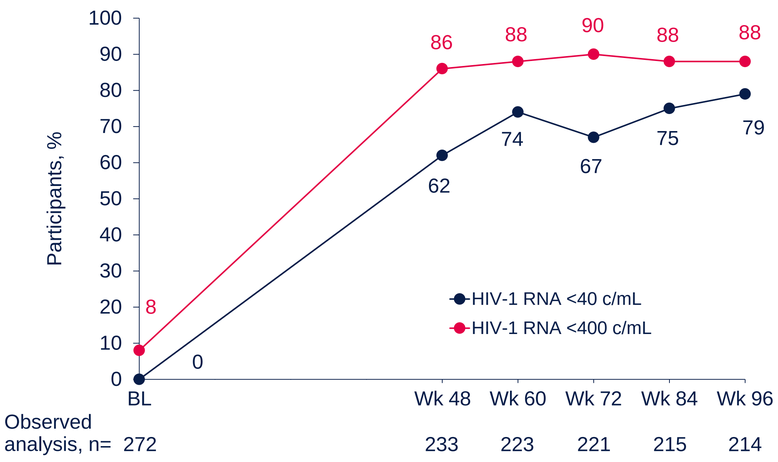
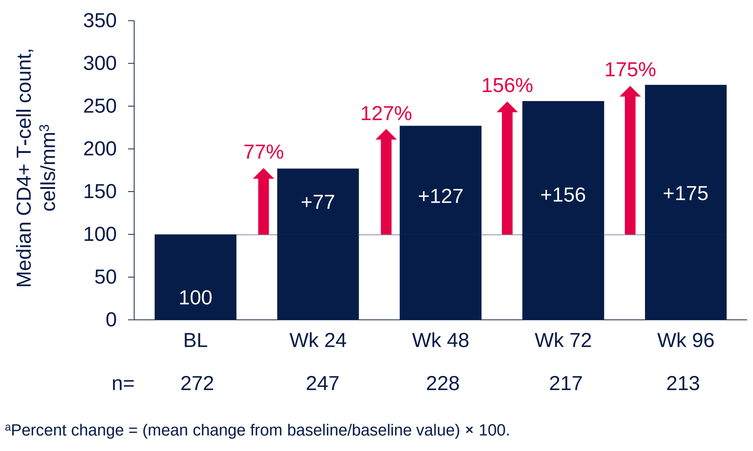
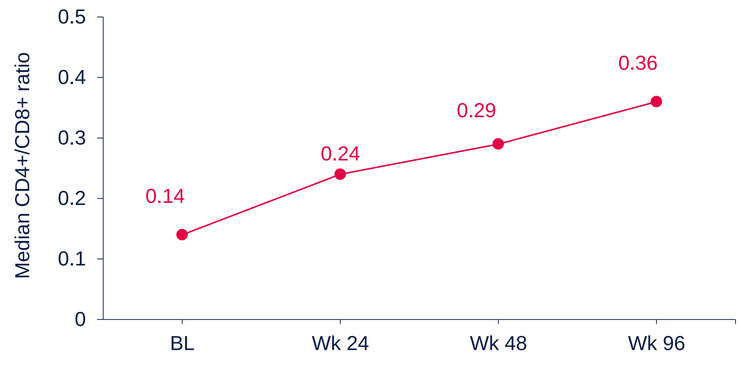


Figure 2. Median CD4+ T-cell Count Increase and Percent Change[a] Through Week 96: BRIGHTE Randomized Cohort



[a]Percent change = (mean change from baseline/baseline value) × 100.

Figure 3. Median CD4+/CD8+ Ratio Through Week 96: BRIGHTE Randomized Cohort



VIKING-3 Virologic Outcomes

- In the intention-to-treat–exposed population, 69% and 63% had HIV-1 RNA <50 c/mL (Snapshot) at Weeks 24 and 48, respectively
- By observed analysis, the proportion of participants with virologic response was high at Week 48 and sustained through Week 96 (Figure 4)

VIKING-3 Immunologic Outcomes

- Improvements in CD4+ T-cell count (Figure 5) and CD4+/CD8+ ratio (Figure 6) were observed through Weeks 96 and 48, respectively

VIKING-3 Safety

- AEs were reported in 92% (169/183) of participants
- Through Week 96, serious AEs were reported in 25% (46/183) of participants; 1% (2/183) were drug-related
  - Serious AEs were most commonly reported from the infections and infestations system organ class
- AEs leading to discontinuation were reported in 4% (8/183) of participants

Figure 4. Virologic Response Through Week 96 by Observed Analysis: VIKING-3

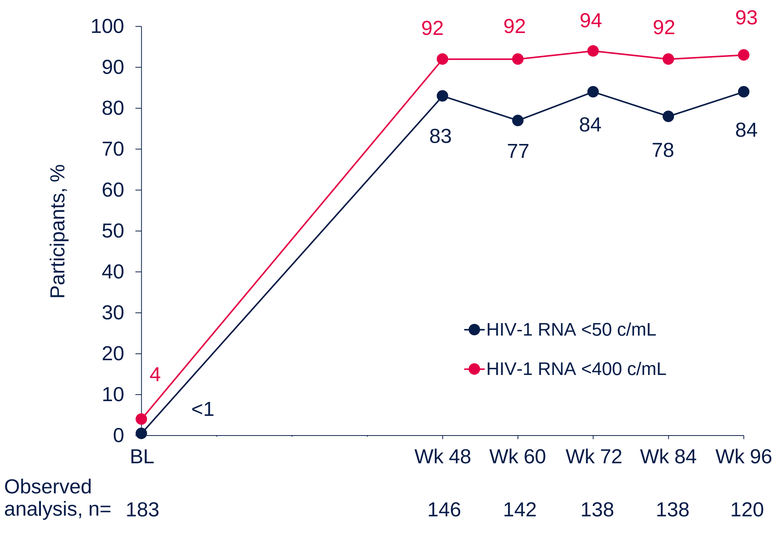
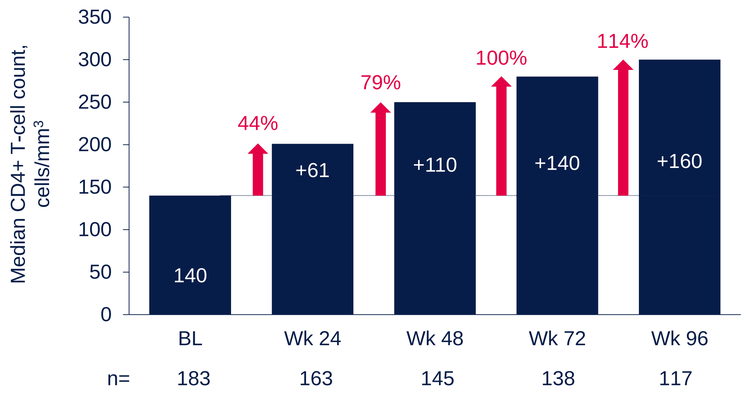
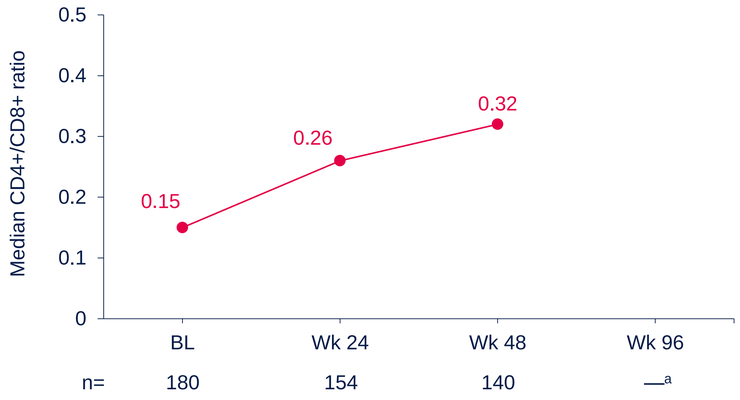


Figure 5. Median CD4+ T-cell Count Increase and Percent Change[a] Through Week 96: VIKING-3



[a]Percent change = (mean change from baseline/baseline value) × 100.

Figure 6. Median CD4+/CD8+ Ratio Through Week 48: VIKING-3



[a]Analysis not performed as CD8+ T-cell count data were not collected after Week 48.

Conclusions

- Despite limited ARV options for individuals living with MDR HIV-1, over 96 weeks, both FTR- and DTG (BID)-based regimens provided robust virologic suppression and improvement in CD4+ T-cell count and CD4+/CD8+ ratio
- While VIKING-3 was conducted from 2011 to 2015 and BRIGHTE was initiated in 2015 and remains ongoing, both studies employed a similar design (eg, short ~1-week functional monotherapy period with investigational drug + failing regimen, followed by investigational drug + OBT, with no active comparators)
- Although differences in baseline characteristics existed, immunosuppression at baseline was more profound in participants from the BRIGHTE study
- FTR and DTG were commonly used together in BRIGHTE, engaging different mechanisms of action
  - 84% of BRIGHTE participants used DTG in initial OBT
- Results from the phase 3 BRIGHTE and VIKING-3 studies provide further support that effective regimens can be constructed for individuals living with MDR HIV-1

Presenting author: Antonella Castagna; castagna.antonella@hsr.it