Rukobia and Immunologic Recovery in the BRIGHTE Study

Summary

- BRIGHTE is an ongoing, phase 3 study evaluating *Rukobia* (fostemsavir [FTR]) in heavily treatment-experienced (HTE) adults with multi-drug resistant HIV-1[1]
  - To view the full MI letter and an overview of the BRIGHTE study, click here.
- Change from baseline in CD4+ T-cell count through Week 240 in the randomized cohort is a secondary endpoint of the BRIGHTE study.[2]
  - CD4+ T-cell counts increased steadily over time, reaching a mean increase of 296 cells/mm^3 at Week 240 in the randomized cohort.[3]
  - Patients with a baseline CD4+ T-cell count < 20 cells/mm^3 experienced the greatest numerical increase through Week 240.[3]
- Important safety information is found in the attached Prescribing Information.

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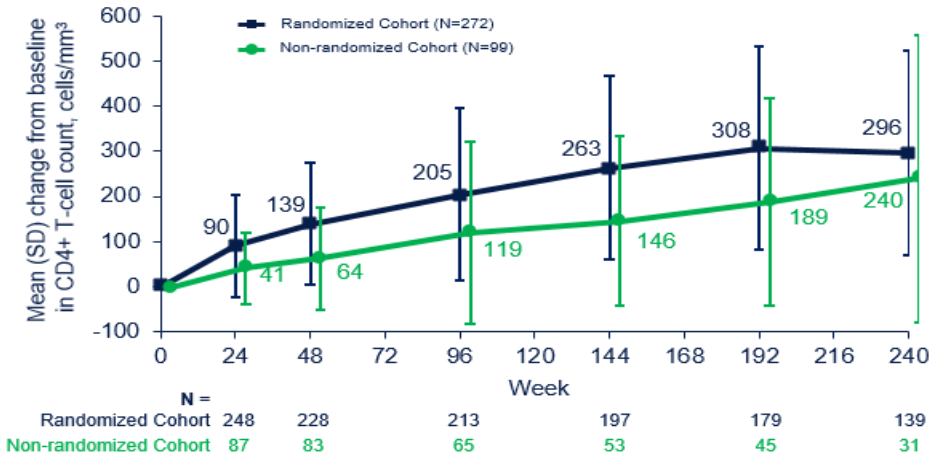
CHANGE IN CD4+ T-CELL COUNT AT DAY 8 (RANDOMIZED COHORT)

Increases in CD4+ T-cell count at Day 8 in the FTR and placebo groups over the blinded period were similar, with mean increases of 18.4 cells/mm^3 and 19.0 cells/mm^3, respectively.[2]

CHANGE IN CD4+ T-CELL COUNT OVER TIME

CD4+ T-cell counts increased steadily over time, reaching a mean increase of 296 cells/mm^3 at Week 240 in the randomized cohort.[3]

Figure 1. CD4+ T-Cell Response through Week 240[3]



IMMUNOLOGIC RESPONSE BY SUBGROUP

In general, comparable immunologic improvements occurred across subgroups analyzed.[2] Patients within the randomized cohort who were most immunocompromised at baseline (CD4+ T-cell count < 20 cells/mm^3) experienced the greatest numerical increases in CD4+ cell count through Week 240.

Figure 2. Change in CD4+ T-Cell Count From Baseline to Week 240 by Virologic Response at the Same Time Point (Randomized Cohort, Observed Analysis)[3]

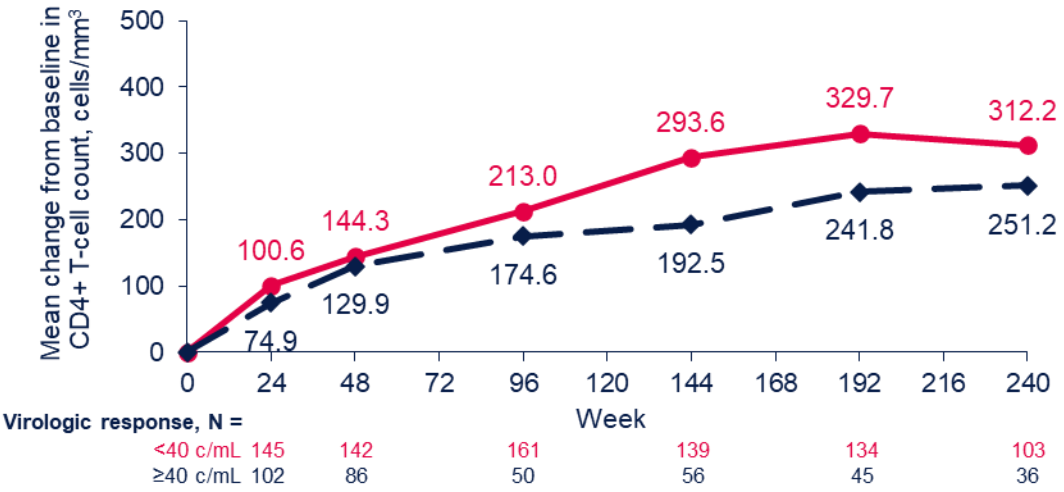
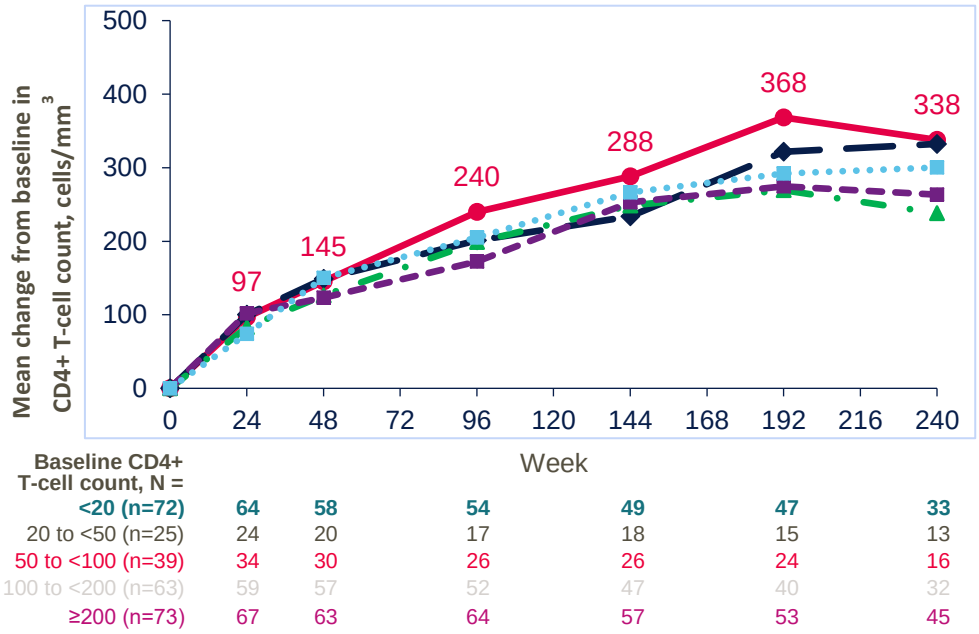


Figure 3. Change in CD4+ T-Cell Count Through Week 240 By Baseline CD4+ Category (Randomized Cohort)[3]



The overall proportion of patients with a CD4+ T-cell count ≥ 200 cells/mm³ at Week 96 was 76% and 48% in the randomized and non-randomized cohorts, respectively.[2] In the Randomized Cohort between baseline and Week 240, 73/94 (78%) participants had a change in CD4+ T-cell count from <200 to ≥200 cells/mm³, and 22/33 (67%) had a change from <20 to ≥200 cells/mm³.[3]

In both cohorts, patients with HIV-1 RNA < 400 copies/mL experienced immune recovery similar to patients with HIV-1 RNA < 40 copies/mL (see Table 1).[2] Of patients in the randomized cohort with HIV-1 RNA ≥ 40 copies/mL or ≥ 400 copies/mL, the mean increase in CD4+ T-cell count was 74.9 cells/mm³ and 50.3 cells/mm³, respectively, at Week 24 and 172.1 cells/mm³ and 130.2 cells/mm³ , respectively, at Week 96.

Table 1. CD4+ T-Cell Count Change from Baseline Over Time by Snapshot Outcome - ITT-E[2]

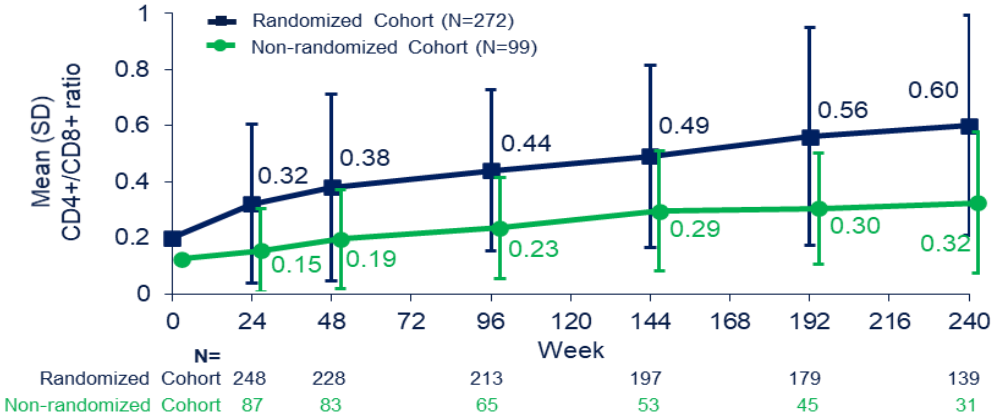
Timepoint/Outcome	Randomized Cohort				Non-Randomized Cohort			
	N	n	Mean (SD)	Median (Q1, Q3)	N	n	Mean (SD)	Median (Q1, Q3)
Week 24								
HIV-1 RNA <40 c/mL	144	144	101.0 (112.53)	80.5 (40.0 150.0)	37	35	62.5 (93.59)	38.0 (18.0 96.0)
HIV-1 RNA <200 c/mL	186	186	95.9 (118.27)	82.5 (36.0 144.0)	42	40	71.2 (91.88)	43.5 (22.5 115.5)
HIV-1 RNA <400 c/mL	203	203	98.6 (118.24)	85.0 (35.0 154.0)	44	42	73.8 (90.73)	48.5 (24.0 122.0)
Week 48								
HIV-1 RNA <40 c/mL	146	142	144.3 (133.17)	133.0 (67.0 213.0)	38	38	116.2 (124.85)	103.0 (31.0 176.0)
HIV-1 RNA <200 c/mL	187	183	150.1 (141.15)	141.0 (67.0 219.0)	43	43	116.4 (118.95)	110.0 (31.0 176.0)
HIV-1 RNA <400 c/mL	190	186	150.9 (140.75)	141.0 (68.0 219.0)	44	44	113.5 (119.22)	106.5 (30.5 175.5)
Week 96								
HIV-1 RNA <40 c/mL	163	160	214.1 (192.17)	190.5 (107.5 294.5)	37	36	200.5 (230.44)	147.5 (73.5 220.5)
HIV-1 RNA <200 c/mL	174	171	217.9 (196.04)	189.0 (109.0 300.0)	39	38	194.9 (225.87)	147.5 (72.0 219.0)
HIV-1 RNA <400 c/mL	175	172	220.7 (198.84)	190.5 (110.0 303.0)	40	39	189.7 (225.25)	144.0 (69.0 219.0)

c/mL = copies/mL; ITT-E = intent-to-treat exposed; SD = standard deviation.

CHANGE IN CD4+/CD8+ T-CELL COUNT RATIO OVER TIME

Both cohorts had extremely low CD4+/CD8+ mean ratios at the start of the BRIGHTE study, with lower values in the non-randomized cohort.[2] Ratios increased over time in both cohorts. Among randomized patients, there was a steady increase in mean ratio at Week 240 (from 0.2 to 0.6).[3]

Figure 4. CD4+/CD8+ Ratio Through Week 240 (Observed Analysis)[3]



Some information contained in this response may not be included in the approved Prescribing Information. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling.

In order for ViiV Healthcare to monitor the safety of our products, we encourage healthcare

professionals to report adverse events or suspected overdoses to the company at 877–844–8872. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCES

1. Kozal M, Aberg J, Pialoux G, et al. Fostemsavir in Adults with Multidrug-Resistant HIV-1 Infection. *New England Journal of Medicine*. 2020;382(13):1232-1243. doi:http://dx.doi.org/10.1056/NEJMoa1902493.
2. Data on File. Study 205888 (NCT02362503). ViiV Healthcare Study Register. Study entry at: https://www.viiv-studyregister.com/en/study/?id=205888.
3. Aberg J, et al. Efficacy and Safety of Fostemsavir Plus Optimized Background Therapy in Heavily Treatment-Experienced Adults With HIV-1: Week 240 Results of the Phase 3 BRIGHTE Study. Presented at AIDS 2022, July 29-August 2, 2022, Montreal, Canada, and virtually. E-poster. EPB160.