Poster 0540

HIV Viral Blips in Adults Treated with INSTI-Based Regimens Through 144 Weeks

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Background

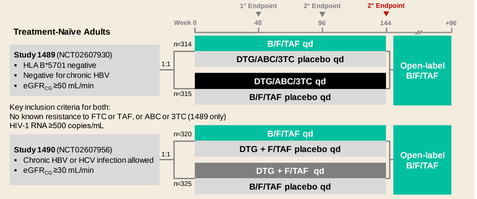
- The single tablet regimen bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guidelines-recommended regimen with demonstrated safety and efficacy and a high barrier to resistance[1-5]
- Studies 1489 and 1490 are two phase 3 studies of B/F/TAF compared with dolutegravir (DTG)-containing regimens in treatment-naïve adults
  - B/F/TAF was non-inferior to DTG/ABC/3TC and DTG + F/TAF through 144 weeks of treatment[6]
- Viral blips are transient elevated viral load values that generally do not affect clinical outcomes
- Variability of HIV-1 RNA assays is high at lower viral loads; many blips that are <200 c/mL may be due to assay error[7]
  - DHHS guidelines use a threshold of ≥200 c/mL as evidence of virologic failure[3]
- Treatment guidelines define virologic suppression as maintenance of HIV-1 RNA <50 c/mL; however, some HIV-1 RNA assays have a lower limit of quantification of 20 c/mL and viral loads from 20-50 c/mL can now be studied

Objectives

- Compare the frequency of viral blips among participants on the INSTI-based regimens B/F/TAF, DTG/ABC/3TC, and DTG + F/TAF
- Assess the impact of viral blips on clinical outcomes using these regimens

Methods

Figure 1. GS-US-380-1489/1490 Study Designs



eGFR$_{CG}$, estimated glomerular filtration rate by Cockcroft-Gault equation; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen.

- Participants with at least one on-treatment post-baseline HIV-1 RNA value were included in this analysis
  - All on-treatment HIV-1 RNA data through Week 144 were included
- Viral blips were defined as an HIV-1 RNA value ≥50 c/mL preceded and followed by HIV-1 RNA <50 c/mL, after achieving confirmed suppression (two consecutive HIV-1 RNA values <50 c/mL)
- Plasma HIV-1 RNA was measured using the Roche COBAS Taqman 2.0 test, which provides quantitative results above 20 c/mL
- Virologic outcomes at Week 144 were measured by the last on-treatment observation carried forward (LOCF) method
- An exploratory analysis of very low-level viral blips ≥20 c/mL and their effect on clinical outcome was also performed

Results

Figure 2. Viral Blip Analysis Participant Classification

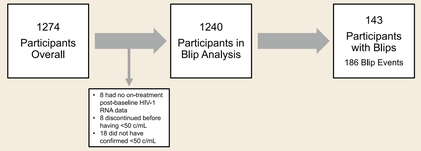


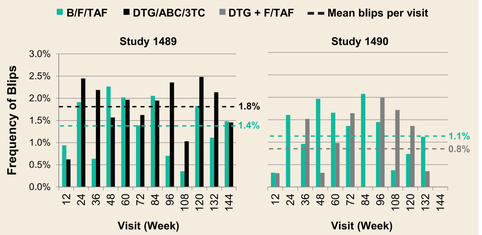
Table 1. Viral Blips Through Week 144

	Study 1489		Study 1490		All N=1240
	B/F/TAF n=308	DTG/ABC/3TC n=309	B/F/TAF n=306	DTG + F/TAF n=317	
Experienced Blips, % (n)	12.4% (39)	15.6% (49)	10.2% (32)	7.1% (23)	11.5% (143)
P-value[a]	0.3		0.2		
Experienced Multiple Blips, % (n)	2.9% (9)	3.6% (11)	2.3% (7)	1.9% (6)	2.7% (33)
Number of Blip Events	49	66	40	31	186
P-value[b]	0.53		0.55		
Participants with Blips <200 c/mL	5.8% (18)	5.5% (17)	6.2% (19)	3.5% (11)	5.2% (65)
Participants with Blips ≥200 c/mL	6.8% (21)	10.4% (32)	4.2% (13)	3.8% (12)	6.3% (78)
Participants with Blips per Study Visit, %	1.4%	1.8%	1.1%	0.8%	1.3%

a. Fisher's exact test
b. Two sample t-test with unequal variance assumption, comparing number of blips per participant

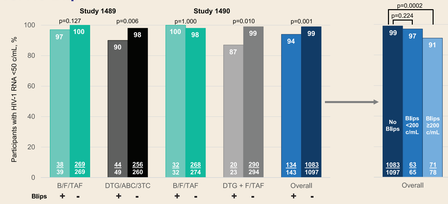
- Similar proportions of participants experienced blips in all treatment groups
- The proportions of participants with blips <200 c/mL or ≥200 c/mL were similar between treatment groups

Figure 3. Frequency of Viral Blips by Study Visit Through Week 144



- An average of 1.3% of participants experienced a blip per study visit, and this was similar between treatment arms

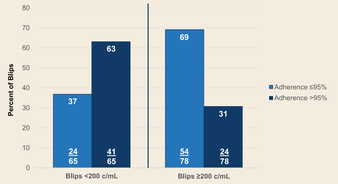
Figure 4. Week 144 LOCF Outcomes of Participants with Blips vs. No Blips



p-values were determined by Fisher's exact test

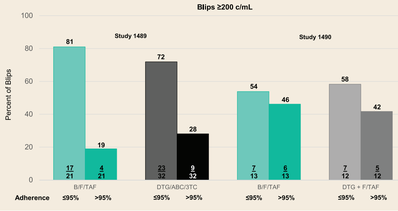
- In the B/F/TAF group, there was no difference in efficacy between participants with or without blips
  - Efficacy was significantly lower in participants with blips in each DTG-based regimen compared to those without blips
- Overall, virologic suppression at Week 144 was lower in participants with blips ≥200 c/mL than in those without blips

Figure 5. Blips and Adherence Level



- Low-level blips <200 c/mL were observed with high adherence >95%; many of these blips may be due to assay variation[7]
- High-level blips ≥200 c/mL were observed with cumulative adherence ≤95%

Figure 6. Blips ≥200 c/mL and Adherence Level



- High-level blips ≥200 c/mL were more common in participants with cumulative adherence ≤95% in all treatment groups

Table 2. Resistance Analysis Population; Full Analysis Set

	Study 1489		Study 1490	
	B/F/TAF n=314	DTG/ABC/3TC n=314	B/F/TAF n=313	DTG + F/TAF n=325
Resistance Analysis Population, n	0	7	8	6
With blips	0	3	0	2
Emergent Resistance to Study Drugs	0	0	0	0

- No participant had emergent resistance to study drugs

Table 3. Very Low-Level Viral Blips ≥20 c/mL Through Week 144

- An exploratory analysis of very low-level viral blips ≥20 c/mL was performed. Very low-level viral blips were defined as an HIV-1 RNA value ≥20 c/mL preceded and followed by HIV-1 RNA <20 c/mL, after achieving confirmed suppression to <20 c/mL (two consecutive HIV-1 RNA values <20 c/mL).

	Study 1489		Study 1490		All N=1227[a]
	B/F/TAF n=304	DTG/ABC/3TC n=306	B/F/TAF n=301	DTG + F/TAF n=316	
Experienced Very Low-Level Blips, % (n)	27.3% (83)	33.3% (102)	25.2% (76)	28.8% (91)	28.7% (352)
P-value[b]	0.1		0.4		
Number of Very Low-Level Blip Events	101	143	100	117	461
Participants with Very Low-Level Blips ≥20-50 c/mL	20.1% (61)	21.2% (65)	19.9% (60)	24.4% (77)	21.4% (263)
Participants with Blips ≥50-200 c/mL	3.0% (9)	3.9% (12)	3.7% (11)	1.9% (6)	3.1% (38)
Participants with Blips ≥200 c/mL	4.3% (13)	8.2% (25)	1.7% (5)	2.5% (8)	4.2% (51)
Participants with Very Low-Level Blips per Visit, %	2.6%	3.7%	2.7%	3.0%	3.0%
Week 144 LOCF Outcome, % with HIV-1 RNA <50 c/mL					
Participants with Very Low-Level Blips ≥20-50 c/mL	100% (61/61)	98% (64/65)	100% (60/60)	100% (77/77)	99% (262/263)
Participants with No Blips ≥20 c/mL	100% (221/221)	99% (201/204)	98% (221/225)	98% (221/225)	99% (864/875)
P-value, very low-level blips ≥20-50 c/mL vs. no blips[b]	1.000	1.000	0.582	0.576	0.315

a. Of the 1274 participants overall in Studies 1489 and 1490, 8 had no on-treatment post-baseline HIV-1 RNA data; 19 discontinued before having <20 c/mL; and 20 did not have confirmed <20 c/mL, leaving N=1227 participants in this analysis
b. Fisher's exact test

- Similar proportions of participants experienced very low-level blips of 20-50 c/mL in all treatment groups
- Very low-level blips of 20-50 c/mL did not affect virologic outcome

Conclusions

- Viral blips were infrequent and similar among participants treated with B/F/TAF, DTG/ABC/3TC, or DTG + F/TAF, with an average of 1.3% of participants having a blip per study visit
- Blips did not affect viral suppression at Week 144 for the B/F/TAF group, but lower suppression was seen in those with blips in the DTG-based regimen groups
  - Overall, having a blip ≥200 c/mL was associated with lower suppression at Week 144; however, this result may be driven by those with adherence ≤95%
- There was no resistance development on any of these BIC- or DTG-containing 3-drug regimens
- Very low-level blips of 20-50 c/mL were comparable across treatment groups and did not affect virologic outcome

References

1. BIKTARVY® (bictegravir, emtricitabine, and tenofovir alafenamide) Tablets for Oral Use Prescribing Information. Gilead Sciences, Initial US Approval 2018.
2. Biktarvy: EPAR – Product Information. European Medicines Association, 2018.
3. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. DHHS, December 2019.
4. EACS Guidelines Version 10.0, November 2019.
5. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults. IAS-USA, 2018.
6. Orkin C, et al. Lancet HIV, 2020.
7. White KL, et al. AIDS, 2018: 1053-1057.

Acknowledgments

We extend our thanks to the participants and their families, study investigators and staff.

These studies were funded by Gilead Sciences, Inc.

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Presented at the Conference on Retroviruses and Opportunistic Infections, Boston, MA, March 8-11, 2020

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