Poster 0540

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

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Background

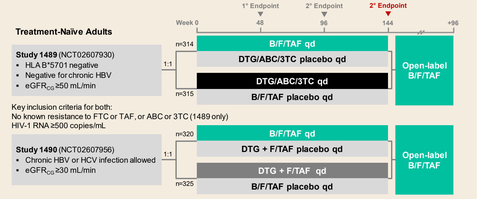
- The single tablet regimen bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guidelines-recommended regimen with demonstrated safety and efficacy and a high barrier to resistance[1-5]
- Studies 1489 and 1490 are two phase 3 studies of B/F/TAF compared with dolutegravir (DTG)-containing 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

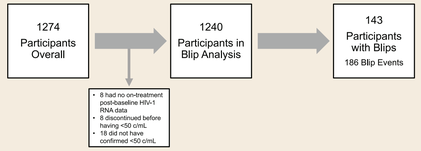


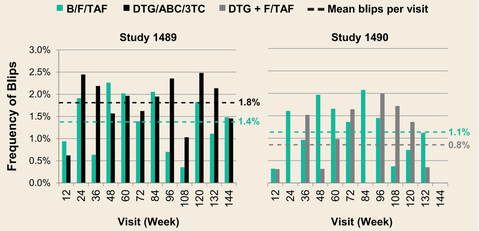
Table 1. Viral Blips Through Week 144

	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

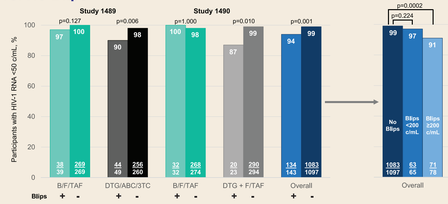
- Similar proportions of participants experienced blips in all treatment groups
- The proportions of participants with blips <200 c/mL or ≥200 c/mL were similar between treatment groups

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

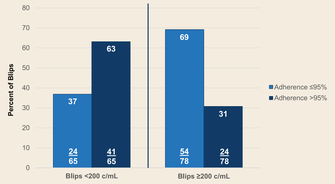
Figure 4. Week 144 LOCF Outcomes of Participants with Blips vs. No Blips



p-values were determined by Fisher's exact test

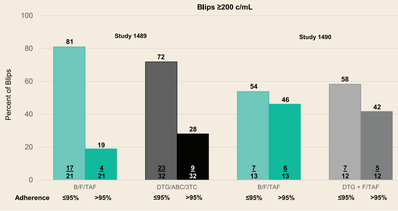
- In the B/F/TAF group, there was no difference in efficacy between participants with or without blips
  - Efficacy was significantly lower in participants with blips in each DTG-based regimen compared to those without blips
- Overall, virologic suppression at Week 144 was lower in participants with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

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Acknowledgments

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