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## BACKGROUND

- Clinical trials demonstrated the robustness and the high efficacy of Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF).
- Real-world evidence data in people living with HIV-1 (PLH) experiencing virologic failure (VF) on B/F/TAF remains limited, especially on emerging resistance associated mutations (RAMs).
- Objective:** To retrospectively describe the virological outcomes in pre-treated PLH who experienced VF on B/F/TAF, based on their genotypic data and their viral load at treatment initiation

## METHODS

- HIV-1 adults from the regional prospective cohort ANRS-CO3-AquiVIH-NA (France) treated with B/F/TAF between 2018/01/01 and 2021/12/31 were included if they had:
  - a HIV-1 viral load (VL) available within 1 year
  - a CD4 measurement available within 2 years
  - at least one genotypic resistance test (GRT) available before B/F/TAF initiation.
- Virological data:
  - VF was defined as either 2 consecutive HIV-1 viral loads (VL)>50 copies/mL or 1 VL>200 copies/mL
  - GRTs were performed using Sanger sequencing as part of standard clinical care. RAMs were reported according to the v34 ANRS resistance algorithm (<https://hivfrenchresistance.org/>).
  - Virological outcomes at the last follow-up visit: B/F/TAF discontinuation/ continuation, last VL

## RESULTS

### Study population



Emergence of resistance occurred for 6/66 (9.1%) pre-treated PLH with documented virological failure on B/F/TAF. Viral suppression was observed on 71.4% PLH following B/F/TAF despite previous VF, suggesting that the main cause of VF on this regimen could be due to poor adherence issues.

### Characteristics of PLH experiencing Virological Failure

	PWH with baseline VL<50 n= 31	PWH with baseline VL>50 N= 35	PWH total N=66
Age, years, median [min-max]	48.8 [23.8-68.6]	54.6 [30.8-74.4]	54.4 [23.8-74.4]
Previous cART, number of lines	3 [1-12]	7 [1-13]	4 [1-13]
Previous VF, n (%)	21 (67.7)	35 (100)	56 (84.8)
Baseline VL, copies/mL, median [min-max]	28 [0-49]	140 [53-599,503]	57 [0- 599,503]
Baseline CD4, cells/µL, median [min-max]	669 [93-1721]	622 [41-1630]	638 [41-1721]
Baseline B/F/TAF RAMs providing resistance to: n (%):			
3TC/FTC	8 (25.8)	16 (45.7)	24 (36.4)
TDF/TAF	3 (9.7)	5 (14.3)	8 (12.1)
BIC	0 (0.0)	0 (0.0)	0 (0.0)
VF VL <sup>1</sup> , copies/mL, median [min-max]	640 [52-567,564]	213 [57-340,000]	258 [52-567,564]
Delay before VF <sup>2</sup> , months [min-max]	16 [2-59]	13 [5-54]	13 [2-59]

<sup>1</sup> 2<sup>nd</sup> VL > 50 copies/mL measurement or 1<sup>st</sup> VL measurement >200 copies/mL. <sup>2</sup> delay between B/F/TAF initiation and 2<sup>nd</sup> VL > 50 copies/mL or 1<sup>st</sup> VL >200 copies/mL.

### Emerging RAMs of PLH with baseline VL>50 copies/mL

#	Clade	Baseline RAMs				VF RAMs				
		VL (copies/mL)	previous NRTI RAMs	Previous INSTIs RAMs	GSS	Delay to VF (months)	VL (copies/mL)	VF NRTI RAMs	VF INSTIs RAMs	GSS*
1	B	95	0	No data	3	13	297	0	0	3
2	B	8530	184V	0	2	10	304	0	0	3
3	B	140	184V	No data	2	35	578	184V	0	2
4	B	599,503	184V	No data	0	0	No data	No data	ND	ND
5	B	322	41L, 74V, 184V, 215FL	No data	1,5	46	4,520	70K1, 184VM, 215FL	0	2
6	B	238	0	0	3	6	181	GRT failed	0	3
7	B	81	41L, 210W, 215Y	0	2,5	6	263	0	0	3
8	B	72	69NS, 70R, 184V	0	2	12	67	69NS, 70RK, 184VM	0	2
9	B	260	0	0	3	11	156	0	0	3
10	B	127	184V	0	2	43	126	No data	No data	ND
11	B	7,310	41L, 184V, 210W, 215Y	0	1,5	11	48,400	0	0	3
12	B	58	41L, 184V, 210W, 215Y	0	1,5	16	74	No data	No data	ND
13	B	371	0	0	3	54	77	184V	GRT failed	2
14	01_AE	123,000	0	No data	3	22	22,800	0	0	3
15	B	192	184V	0	2	13	69	0	0	3
16	B	125,000	69N, 184IM	0	2	45	100,000	0	0	3
17	B	55	0	0	3	15	340,000	0	0	3
18	B	75	210W 215D	0	3	6	91	210W 215D	GRT failed	3
19	B	58	0	No data	3	35	69	0	0	3
20	G	67	184V	0	2	19	232	0	0	3
21	URF	778	0	0	3	7	312	0	0	3
22	B	86	0	0	3	12	121	0	0	3
23	B	53	41L, 67N, 184V, 210W, 215Y	0	1	5	190	GRT failed	0	3
24	URF	273,000	67N 184V T215I K219Q	0	2	11	213	184V	263K	1
25	B	257	0	0	3	19	190	No data	No data	ND
26	B	80	67N 184V 210W 215Y	0	1,5	12	139	0	GRT failed	3
27	F1	94	0	0	3	17	88	0	0	3
28	02_AG	356	184V	0	2	8	95	184VM	0	2
29	B	68,900	41W, 184V, 215TA	0	2	17	18,200	0	0	3
30	F1	12,400	0	0	3	14	146,172	0	0	3
31	B	87	0	0	3	11	89	0	GRT failed	3
32	D	109	44D	0	3	8	128	GRT failed	0	3
33	02_AG	146	210M	0	3	15	247	210M	0	3
34	A2	90	69N	0	3	22	271	0	0	3
35	B	79	41LM, 44KE, 67ND, 215DA	0	3	7	219	GRT failed	0	3

ND: not determined; GSS: Genotypic Sensitivity Score (Sensitivity = 1; partially resistant = 0.5; resistant = 0). \*GSS at VF was calculated according to VF GRT

### Emerging RAMs of PLH with baseline VL<50 copies/mL

#	Clade	Baseline RAMs			VF RAMs				
		Previous NRTI RAMs	Previous INSTIs RAMs	GSS	VF VL (copies/mL)	Delay to VF (months)	VF NRTI RAMs	VF INSTIs RAMs	GSS*
36	B	41L, 184IM, 215EK	0	2	20,940	12	No data	No data	ND
37	02_AG	0	No data	3	35,065	3	No data	No data	ND
38	B	69TA	0	3	4,410	8	GRT failed	0	3
39	02_AG	67G, 70T, 184V, 215F	74ML, 97A	2	32,400	13	GRT failed	0	3
40	B	0	0	3	52	30	No data	No data	ND
41	B	0	0	3	567,564	20	No data	No data	ND
42	A1	0	0	3	9,350	36	GRT failed	0	3
43	B	0	0	3	145	12	No data	No data	ND
44	B	41L, 184V, 210W, 215Y	No data	1,5	289	25	No data	No data	ND
45	B	0	0	3	239	6	No data	No data	ND
46	13_cpx	69TI	74I, 145PS	3	253	34	No data	No data	ND
47	URF	0	0	3	761	3	No data	No data	ND
48	URF	0	0	3	446	9	No data	No data	ND
49	URF	69+, 70R, 215N	0	1	199,000	54	69+ 70R, 215N	0	1
50	02_AG	0	0	3	222,000	28	184VM	GRT failed	2
51	B	215NY, 219KN	0	3	89	18	0	0	3
52	B	0	0	3	78	4	184V	0	2
53	B	0	0	3	750	43	184V	155NH	1
54	URF	184I	0	2	4,070	18	0	0	3
55	G	0	0	3	2,230	11	0	0	3
56	A3	0	0	3	1,500	42	0	0	3
57	B	0	0	3	210	2	0	0	3
58	C	0	0	3	640	9	184V	0	2
59	B	0	0	3	210	29	0	0	3
60	B	0	0	3	118	22	0	0	3
61	02_AG	67ND, 69TS, 70RK, 184VM, 219KQ	0	2	110	16	67ND, 69TS, 70R, 184VM, 219Q	0	2
62	B	0	0	3	106	4	0	0	3
63	B	41L, 67N, 70R, 184V, 210W, 215E, 219Q	0	1	293	59	41L, 67N, 70R, 184V, 210W, 215E, 219Q	0	1
64	B	74V, 184V	0	2	926	6	0	0	3
65	B	0	0	3	238	38	0	0	3
66	A1	0	0	3	8,560	11	0	0	3

ND: not determined; GSS: Genotypic Sensitivity Score (Sensitivity = 1; partially resistant = 0.5; resistant = 0). \*GSS at VF was calculated according to VF GRT

### Follow-up of PLH after Virological failure

- B/F/TAF was maintained for 56 participants (including #13, #50 and #52 with emerging M184V) and 40 of them (71.4%) had a HIV-1 VL <50 copies/mL at their last visit.
- ARV treatment was modified to PI- or NNRTI-based regimens for 6 participants (# 23, 24, 26, 34, 53 and 58); Doravirine was added to B/F/TAF for 1 (#35)
- No follow-up was available for 3 participants: #17 was lost for follow-up and #29 and #30 died

## CONCLUSIONS

- Among PLH with documented VF on B/F/TAF, emergence of resistance occurred in 6/66 (9.1%). Selected RAMs were five M184V, one N155H and one R263K. Preexisting NRTIs RAMs did not seem to enable additional RAMs at failure.
- Poor or inconsistent adherence may explain most of VF cases, as 71.4% of participants pursuing B/F/TAF after VF achieved viral suppression. This emphasizes the importance of adherence counselling in improving outcomes.

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