Predictive factors of virological failure after switching to B/F/TAF (ANRS-CO3-AquiVIH-NA)

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BACKGROUND

- B/F/TAF is a single-tablet regimen recommended by HIV-1 treatment guidelines as a first-line therapy or switch option.
- Limited real-world data exist on its efficacy, tolerability, and persistence, particularly in relation to Pre-existing Mutations (PRMs).

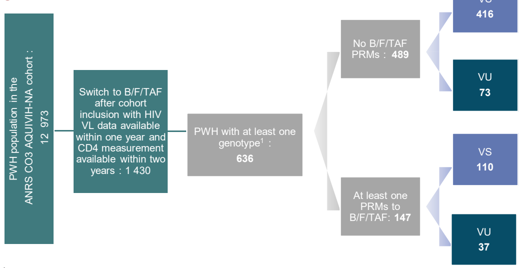
OBJECTIVE

- To evaluate in the ANRS CO3 AQUIVIH-NA cohort, the occurrence of virological failure (VF) after B/F/TAF initiation according to:
  - viral load (VL) at treatment initiation
  - presence of PRMs

METHODS

- We conducted a **retrospective study** within the ANRS-CO3-AquiVIH-NA cohort, a French regional prospective cohort of people with HIV (PWH) followed in 15 hospitals in southwestern France. Since 1987, the cohort has collected clinical and biological data, with a biobank established in 2008. PWH who initiated B/F/TAF treatment between January 1, 2018, and December 31, 2021 were included. We followed them until discontinuation or lost of information.
- **Study Groups**:
  - Virologically suppressed (VS): VL< 50 copies/mL when switching to B/F/TAF initiation.
  - Virologically unsuppressed (VU): VL > 50 copies/mL when switching to B/F/TAF initiation.
- **Resistance Analysis:**
  - PRMs prior to B/F/TAF initiation were identified using RNA/DNA genotypic resistance tests interpreted according to the ANRS|MIE resistance algorithm (https://hivfrenchresistance.org/)).
- **Virologic Failure (VF) Definition:**
  - Two consecutive VL > 50 copies/mL and <1000 copies/ml or a single VL > 1000 copies/mL within a 60-month follow-up period. In addition, for VU study group, absence of a VL<50 in the first 12 months after switch.
- **Statistical Analysis:**
  - Aalen Johansen survival curves were generated for representation of time to VF.
  - Cox proportional hazards model was used to assess factors associated with VF.

DESIGN


PWH population in the ANRS CO3 AQUIVIH-NA cohort : 12 973
Switch to B/F/TAF after cohort inclusion with HIV VL data available within one year and CD4 measurement available within two years : 1 430
PWH with at least one genotype¹ : 636
No B/F/TAF PRMs : 489
At least one PRMs to B/F/TAF: 147
VS 416
VU 73
VS 110
VU 37

[1] *Participants with available resistance and with viral load data within 21 months after the switch*

RESULTS

PRMs at B/F/TAF initiation

PRMs were detected for **147/636** (23.1%) with:

- M184V/I for 131/147 (89.1%) impacting 3TC and FTC
- 11/147 (7.5%) had 3 or more TAMs and no other mutations impacting ABC, TDF and TAF
- No mutation impacting BIC or DTG

Most common PRMs (in > 1% of participants)	Participants with PRMs, n (%)		
	Total N = 147	VU N = 37	VS N= 110
ALL M184V/I	131 (89.1)	34 (91.9)	97 (88.2)
M184V/I	53 (36.1)	19 (51.4)	34 (30.9)
M184V/I + 1-2 TAMs	30 (20.4)	7 (18.9)	23 (20.9)
M184V/I + 1-2 TAMs + K65R	2 (1.4)	0 (0.0)	2 (1.8)
M184V/I + ≥ 3 TAMs	37 (25.2)	6 (16.2)	31 (28.2)
M184V/I + ≥ 3 TAMs + Q151M	3 (2.0)	0 (0.0)	3 (2.7)
M184V/I + K65R	2 (1.4)	0 (0.0)	2 (1.8)
≥ 3 TAMs	11 (7.5)	2 (5.4)	9 (8.2)

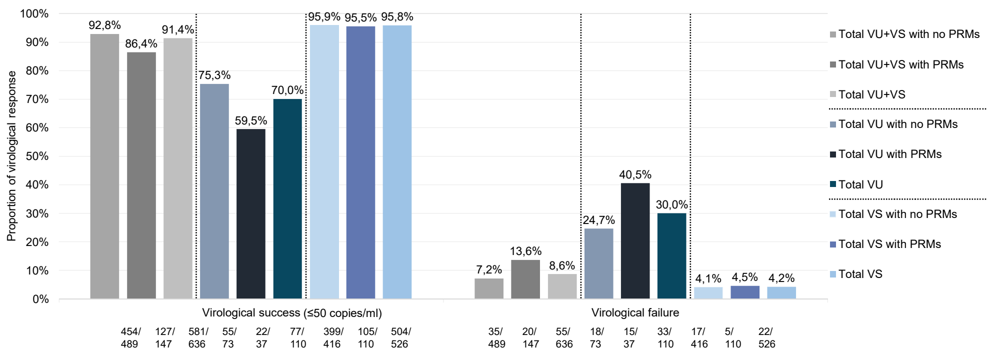
- In virologically suppressed PLWH switching to B/F/TAF, over 95% maintained virologic suppression, regardless of the presence of baseline M184V/I ± 3 TAMs.
- In virologically unsuppressed PLWH switching to B/F/TAF, 70% achieved virologic suppression, including 59.5% with baseline M184V/I ± 3 TAMs and 75.3% without resistance mutations.
- The risk of VF after switching to B/F/TAF was associated with a prior history of VF, prolonged unsuppressed status, high baseline viral load before switching, CD4 count < 350 cells/mm³, and the presence of PRMs and M184V at baseline.

Baseline Characteristics of Participants

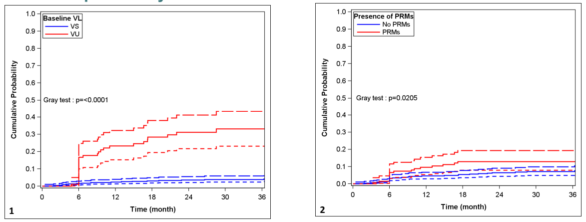
Characteristics	TOTAL[1]			VU			VS		
	no PRMs N= 489	PRMs N= 147	Total N= 636	no PRMs N= 73	PRMs N= 37	Total N= 110	no PRMs N = 416	PRMs N= 110	Total N= 526
Female sex at birth, *n (%)*	123 (25.2)	51 (34.7)	174 (27.4)	30 (41.1)	15 (40.5)	45 (40.9)	93 (22.4)	36 (32.7)	129 (24.5)
Age at B/F/TAF initiation *years, Median (IQR)*	52.0 (44.4;60.1)	**55.6** (48.3;60.6)	52.7 (45.2;60.2)	50.7 (42.9;57.4)	54.1 (48.7;60.3)	51.5 (43.9;59.0)	52.3 (44.5;60.2)	56.7 (48.3;60.6)	53.0 (45.3;60.3)
Contamination group, *n (%)*									
MSM	239 (48.9)	58 (39.5)	297 (46.7)	27 (37.0)	12 (32.4)	39 (35.5)	212 (51.0)	46 (41.8)	258 (49.0) 187
Heterosexuals	185 (37.8)	50 (34.0)	235 (36.9)	33 (45.2)	15 (40.5)	48 (43.6)	152 (36.5)	35 (31.8)	(35.6)
IV drug users	28 (5.7)	27 (18.4)	55 (8.6)	4 (5.5)	5 (13.5)	9 (8.2)	24 (5.8)	22 (20.0)	46 (8.7)
Other	37 (7.6)	12 (8.2)	49 (7.7)	9 (12.3)	5 (13.5)	14 (12.7)	28 (6.7)	7 (6.4)	35 (6.7)
Origin									
France	381 (77.9)	118 (80.3)	499 (78.5)	50 (68.5)	29 (78.4)	79 (71.8)	331 (79.6)	89 (80.9)	420 (79.8)
Sub-Saharan Africa	59 (12.1)	19 (12.9)	78 (12.3)	13 (17.8)	5 (13.5)	18 (16.4)	46 (11.1)	14 (12.7)	60 (11.4)
Other	49 (10.0)	10 (6.8)	59 (9.3)	10 (13.7)	3 (8.1)	13 (11.8)	39 (9.3)	7 (6.4)	46 (8.8)
Time since first HIV serology to switch to B/F/TAF, *years, median (IQR)*	13.3 (6.6;22.4)	**26.1** (21.0;31.1)	16.6 (8.6;25.6)	13.9 (7.1;25.0)	24.2 (18.0;29.1)	17.6 (10.0;26.1)	13.1 (6.6;22.2)	26.9 (22.5;31.5)	16.3 (8.2;25.3)
CD4 count, *cells/μL, median (IQR)*	672 (455;894)	626 (410;820)	669 (446;886)	433 (230;710)	572 (282;809)	489 (230;748)	700 (501;907)	679 (456;821)	690 (486;894)
Stage C (AIDS) of infection, *n (%)*	81 (16.6)	49 (33.3)	130 (20.4)	16 (21.9)	11 (29.7)	27 (24.5)	65 (15.6)	38 (34.5)	103 (19.6)
Number of previous regimens, *median (IQR)*	4 (2;7)	**10** (7;13)	5 (3;9)	4 (2;8)	10 (7;12)	6 (3;10)	4 (2;6)	10 (7;14)	5 (3;8)
Number of prior VF[1], *median (IQR)*	0 (0;2)	**4** (2;8)	1 (0;3)	2 (1;4)	5 (3;7)	3 (1;5)	0 (0;1)	4 (2;8)	1 (0;3)
Reasons for switching to B/F/TAF, *n (%)*									
Non-optimal treatment	302 (59.9)	92 (59.4)	394 (59.8)	34 (45.3)	16 (43.2)	50 (44.6)	268 (62.5)	76 (64.4)	344 (62.9)
Physician choice[2]	116 (23.0)	34 (21.9)	150 (22.8)	13 (17.3)	7 (18.9)	20 (17.9)	103 (24.0)	27 (22.9)	130 (23.8)
Any side-effects	49 (9.0)	10 (6.5)	59 (9.0)	4 (5.3)	1 (2.7)	5 (4.5)	45 (10.5)	9 (7.6)	54 (9.9)
Virological failure	9 (1.8)	5 (3.2)	14 (2.1)	6 (8.0)	3 (8.1)	9 (8.0)	3 (0.7)	2 (1.7)	5 (0.9)
Patient choice	5 (1.0)	5 (3.2)	10 (1.5)	1 (1.3)	2 (5.4)	3 (2.7)	4 (0.9)	3 (2.3)	7 (1.3)
No treatment	23 (4.6)	9 (5.8)	32 (4.9)	17 (22.7)	8 (21.6)	25 (22.3)	6 (1.4)	1 (0.8)	7 (1.3)

[1] After obtaining an HIV RNA < 50 copies/mL: 1 HIV RNA > 1000 copiesp/mL; Or two consecutive HIV RNA > 50 copies/mL and < 1000 copies/mL; Or 1 by line of therapy during a long period of viral load detectability before obtaining the first viral load <50 copies/mL
[2] Including drug reducing

Virological outcomes at the end of the follow-up period

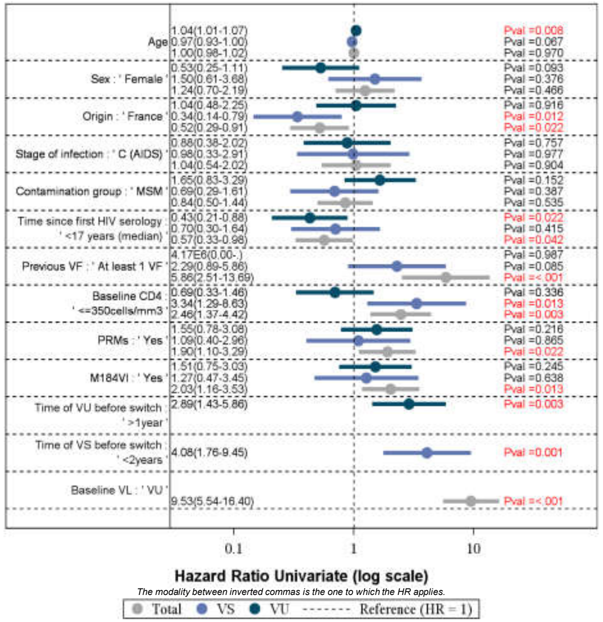

Proportion of virological response
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
92,8%
86,4%
91,4%
75,3%
59,5%
70,0%
95,9%
95,5%
95,8%
7,2%
13,6%
8,6%
24,7%
40,5%
30,0%
4,1%
4,5%
4,2%
Virological success (≤50 copies/ml)
Virological failure
454/489
127/147
581/636
55/73
22/37
77/110
399/416
105/110
504/526
35/489
20/147
55/636
18/73
15/37
33/110
17/416
5/110
22/526
Total VU+VS with no PRMs
Total VU+VS with PRMs
Total VU+VS
Total VU with no PRMs
Total VU with PRMs
Total VU
Total VS with no PRMs
Total VS with PRMs
Total VS

Estimated probability of VF



1- All PWH stratified according to baseline VL (526 VS vs 110 VU). **2-** All PWH stratified according to PRMs (489 noPRMs vs 147 PRMs).

Hazard Ratio (HR) of Factors associated with Virological Failure in Univariate Cox Proportional Hazard Model


Age
1.04(1.01-1.07) Pval =0.008
0.97(0.93-1.00) Pval =0.067
1.00(0.98-1.02) Pval =0.970
Sex : ' Female '
0.53(0.25-1.11) Pval =0.093
1.50(0.61-3.68) Pval =0.376
1.24(0.70-2.19) Pval =0.466
Origin : ' France '
1.04(0.48-2.25) Pval =0.916
0.34(0.14-0.79) Pval =0.012
0.52(0.29-0.91) Pval =0.022
Stage of infection : ' C (AIDS) '
0.88(0.38-2.02) Pval =0.757
0.98(0.33-2.91) Pval =0.977
1.04(0.54-2.02) Pval =0.904
Contamination group : ' MSM '
1.65(0.83-3.29) Pval =0.152
0.69(0.29-1.61) Pval =0.387
0.84(0.50-1.44) Pval =0.535
Time since first HIV serology : ' <17 years (median) '
0.43(0.21-0.88) Pval =0.022
0.70(0.30-1.64) Pval =0.415
0.57(0.33-0.98) Pval =0.042
Previous VF : ' At least 1 VF '
4.17E6(0.00-.) Pval =0.987
2.29(0.89-5.86) Pval =0.085
5.86(2.51-13.69) Pval =< 001
Baseline CD4 : ' <=350cells/mm3 '
0.69(0.33-1.46) Pval =0.336
3.34(1.29-8.63) Pval =0.013
2.46(1.37-4.42) Pval =0.003
PRMs : ' Yes '
1.55(0.78-3.08) Pval =0.216
1.09(0.40-2.96) Pval =0.865
1.90(1.10-3.29) Pval =0.022
M184VI : ' Yes '
1.51(0.75-3.03) Pval =0.245
1.27(0.47-3.45) Pval =0.638
2.03(1.16-3.53) Pval =0.013
Time of VU before switch : ' >1year '
2.89(1.43-5.86) Pval =0.003
Time of VS before switch : ' <2years '
4.08(1.76-9.45) Pval =0.001
Baseline VL : ' VU '
9.53(5.54-16.40) Pval =< 001
0.1
1
10
Hazard Ratio Univariate (log scale)
The modality between inverted commas is the one to which the HR applies.
Total
VS
VU
Reference (HR = 1)

CONCLUSIONS

- In VU+VS PWH treated with B/F/TAF, PRMs were detected in 23.1% *(33,6% in VU; 20,9% in VS)*, including 89.1% with M184V/I mutations *(91,9% in VU; 88,2% in VS)*.
- In VU+VS, Virological failure (VF) with B/F/TAF occurred in 13.6 % of PWH with PRMs *(40,5% in VU and 4,5% in VS)* and 7,2% of PWH without PRMs *(27,7% in VU; 4,1% in VS)*.
- In VU+VS PWH, univariates analysis showed the following factors in the risk of VF:
  - At least one previous VF
  - CD4 count ≤ 350 cells/mm3
  - Baseline VL and of the duration of viral replication before B/F/TAF initiation
  - PRMs
  - M184V/I

ACKNOWLEDGMENTS

Scientific committe : P. Bellecave, P. Blanco, F. Bonnet (Chair), S. Bouchet, D. Breilh, C. Cazanave, S. Desjardin, V. Gaborieau, A. Gimbert, M. Hessamfar, L. Lacaze-Buzy, ME. Lafon, E. Lazaro, O. Leleux., G. Le Moal, D. Malvy, P. Mercié, D. Neau, I. Pellegrin, A. Perrier, V. Petrov-Sanchez, A. Peyrouny-Mazeau, C. Tumiotto, M.O. Vareil, L. Wittkop (Methodologist); *Participating centers :* Hôpital Saint André, CHU de Bordeaux, Médecine Interne et Maladies Infectieuses, (N. Bernard, F. Bonnet, D. Bronnimann H. Chaussade, D. Dondia, P. Duffau, I. Faure, V. Hémar, M. Hessamfar, W. Jourde, C. Martell, P Mercié, A. Monier, P. Morlat, E. Mériglier, F. Paccalin, R. Paz, E. Ribeiro, C. Rivoisy, MA Vandenhende); Hôpital Pellegrin, CHU de Bordeaux, Maladies Infectieuses et Tropicales, (L. Barthod, C. Cazanave, FA. Dauchy, A. Desclaux, H. Dutronc, A. Duvignaud, J. Leitao, D. Neau, D. Nguyen, D. Malvy, T. Pistone, M. Puges, C. Tinevez, C. Vignal, G. Wirth); Hôpital Haut-Lévêque, CHU de Bordeaux, Médecine Interne et Maladies Infectieuses, (C. Courtault, F. Camou, C. Greib, E. Lazaro, JL. Pellegrin, C. Prot-Leurent, E. Rivière, JF. Viallard); Hôpital d'Agen, Médecine Interne (E. Klément-Fructos, A. Nonis, P. Rispal); Hôpital de Libourne, Médecine Interne (O. Caubet, S. De Faucal, M. Favarel-garrigues, H. Ferrand, S. Tchamgoué); Hôpital de Bayonne, Maladies Infectieuses (M. Acquier, L. Alleman, S. Farbos, MO. Vareil, H. Wille); Hôpital de Dax, Médecine Interne et Maladies Infectieuses, (K. André, L. Caunegre, Y. Gérard, M. Lauda-Maillen); Hôpital Saint-Cyr/Villeneuve-sur-Lot, Maladies Infectieuses, (I. Chossat); Hôpital de Mont de Marsan, Médecine Interne et Maladies Infectieuses, (Y. Gerard, F. Lacassin, C. Lasbasses-Depis); Hôpital d'Arcachon, Médecine Interne, (A. Barret, M. Bouet, C. Courtault, M. Roucoules, M. Videcoq); Hôpital de Périgueux, Médecine Interne et Maladies Infectieuses, (C. Belzunce, B. Castan, J. Koffi, N. Rouanes, A. Saunier, J.B. Zabbe); Hôpital de Pau, Médecine Interne et Maladies Infectieuses, (G. Dumondin, V. Gaborieau); Hôpital d'Orthez, Médecine Interne, (Y. Gerard) ; CHU de Poitiers, Médecine Interne et Maladies Infectieuses, (G. Beraud, G. Le Moal, M. Catroux, M. Garcia, V. Giraud, JP. Martellosio, F. Roblot, JM. Turmel) ; Hôpital de Saintes, Médecine Interne, (T. Pasdeloup) ; Hôpital d'Angoulême, Médecine Interne, (A. Riché, M. Grosset, S. Males, C. Ngo Bell) ; Hôpital de Jonzac, Maladies Infectieuses, (T. Pasdeloup), Hôpital de Saint Jean d'Angely, Maladies Infectieuses, (T. Pasdeloup) ; Hôpital de Royan, Médecine Interne, (P. Mottaz, T. Pasdeloup) ; Hôpital de Châtellerault, Médecine Interne (A, Elsendoorn); *Other departements :* Immunology: P. Blanco, I. Pellegrin ; CRB-BBS: C. Carpentier, I. Pellegrin ; Virology: P. Bellecave, C. Tumiotto ; Pharmacology: S. Bouchet, D. Breilh, G. Miremeont-Salamé ; Data collection : G. Amou, A. Barhoumi, P. Camps, S. Delveaux, S. Lawson-Ayayi, E. Lenaud, D. Plainchamps, A. Pougetoux, I. Stagier, B. Uwamaliya, K. Zara; IT department: V. Conte, M. Gapillout ; Project Team : O. Leleux (Project Leader), A. Perrier (Data Manager), A. Peyrouny-Mazeau (Statistitien) ; Participants of the Cohort ANRS CO3-AQUIVIH-NA.

Sponsor: CHU de Bordeaux.
Funding: ANRS|MIE, CHU de Bordeaux and GILEAD Sciences Inc.