Probability of single tablet regimens BIC/FTC/TAF, E/C/F/TAF, RPV/FTC/TAF, DTG/RPV, DTG/3TC or DTG/ABC/3TC discontinuation at 18 months in real life settings in the ANRS-CO3 - AquiVIH-NA cohort.

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Background

- Single tablet regimens (STRs) have revolutionized the management of HIV by providing people living with HIV (PLWH) with a simplified and more convenient treatment approach. By combining multiple antiretroviral drugs into a single tablet, STRs facilitate daily medication adherence, reduce the complexity of treatment regimens, and improve overall treatment adherence.
- In France, STRs have gained popularity over the years and are now widely utilized in HIV care. They account for the majority of prescribed treatments, offering PLWH an effective and convenient therapeutic option.
- However, despite the advantages of STRs in terms of simplicity and adherence, there are still questions and uncertainties regarding their real-world utilization.

Objective

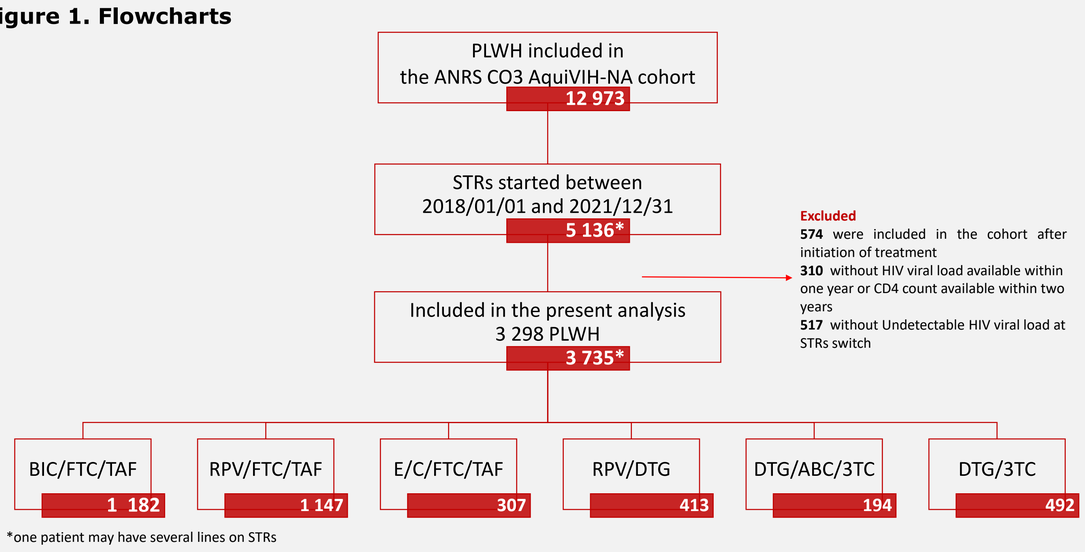
- To describe the probability of STRs discontinuations and virological failure (VF) in suppressed HIV RNA persons who start STRs in real life settings.

Methods

- The ANRS-CO3 - AquiVIH-NA cohort is an open, prospective hospital-based cohort of HIV-1-infected adults (≥18 years old) in care in 15 hospitals in the Nouvelle Aquitaine region of southwestern France.
- The cohort collects epidemiological, clinical, biological and therapeutic data from the medical records of PLWH and who have signed informed consent since 1987.
- We assessed the persistence of switching to major STRs from 01/01/2018 to 12/31/2021 in patients included in the ANRS AQUIVIH-NA cohort with the following criteria :
  - Documented HIV-1 viral load (VL) for at least 12 months prior to switch.
  - Documented CD4 count for at least 24 months prior switching.
  - A suppressed VL (HIV-1 RNA ≤ 50 cp/ml) at the time of switching.
- VF was defined as one HIV-1 RNA >1000 cp/ml VL or two consecutive HIV RNA >50 cp/ml VL and <1000 cp/ml VL during the follow-up period.
- The study analyzed STRs that accounted for over 90% of the STRs initiated during the period.
- Each PLWH may have several sequences of STRs, but was evaluated only once for each STRs initiated during the period.

Results

Figure 1. Flowcharts



*one patient may have several lines on STRs

Table 1. Baseline characteristics of PLWH who switched to a single tablet in the cohort study

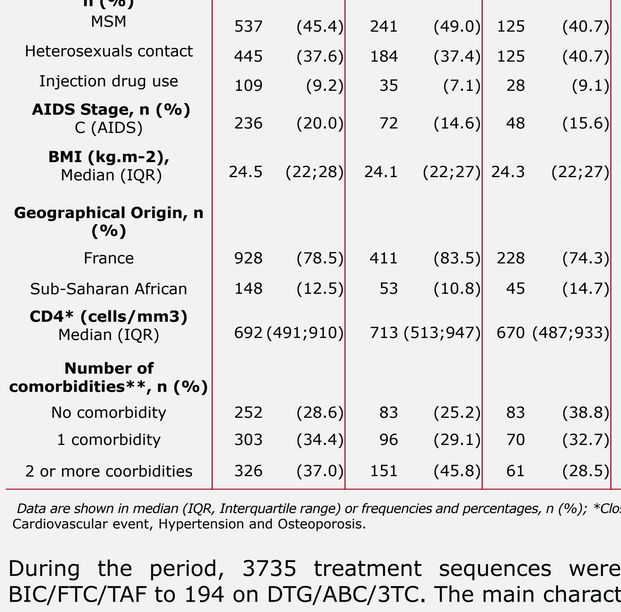
	BIC/FTC/TAF		DTG/3TC		E/C/F/TAF		RPV/DTG		RPV/FTC/TAF		DTG/ABC/3TC		p*	Total	
Characteristics	**N=1182**		**N=492**		**N=307**		**N=413**		**N=1147**		**N=194**			**N=3735**	
Age (in years), Median (IQR)	53.1	(45;60)	54.5	(45;62)	50.5	(39;58)	55.9	(49;62)	50.5	(43;58)	54.6	(46;64)	<0.0001	52.8	(44;60)
Gender, n (%) Women	311	(26.3)	126	(25.6)	90	(29.3)	127	(30.8)	345	(30.1)	64	(33.0)	0,0995	1063	(28.5)
HIV risk group, n (%)													0.0386		
MSM	537	(45.4)	241	(49.0)	125	(40.7)	181	(43.8)	504	(44.0)	78	(40.2)		1666	(44.6)
Heterosexuals contact	445	(37.6)	184	(37.4)	125	(40.7)	162	(39.2)	477	(41.6)	81	(41.8)		1474	(39.5)
Injection drug use	109	(9.2)	35	(7.1)	28	(9.1)	47	(11.4)	74	(6.5)	22	(11.3)		315	(8.4)
AIDS Stage, n (%) C (AIDS)	236	(20.0)	72	(14.6)	48	(15.6)	85	(20.6)	169	(14.7)	43	(22.2)	<0.0001	653	(17.5)
BMI (kg.m-2), Median (IQR)	24.5	(22;28)	24.1	(22;27)	24.3	(22;27)	24.3	(22;27)	24.4	(22;27)	24.3	(22;27)	0.9768	24.4	(22;27)
Geographical Origin, n (%)													0.0001		
France	928	(78.5)	411	(83.5)	228	(74.3)	351	(85.0)	856	(74.6)	152	(78.4)		2926	(78.3)
Sub-Saharan African	148	(12.5)	53	(10.8)	45	(14.7)	33	(8.0)	188	(16.4)	27	(13.9)		494	(13.2)
CD4* (cells/mm3) Median (IQR)	692	(491;910)	713	(513;947)	670	(487;933)	731	(553;960)	706	(528;915)	667	(490;898)	0.0048	703	(510;924)
Number of comorbidities, n (%)**													<0.0001		
No comorbidity	252	(28.6)	83	(25.2)	83	(38.8)	63	(24.3)	252	(34.8)	38	(25.3)		771	(30.1)
1 comorbidity	303	(34.4)	96	(29.1)	70	(32.7)	74	(28.6)	279	(38.5)	38	(25.3)		860	(33.6)
2 or more coorbidities	326	(37.0)	151	(45.8)	61	(28.5)	122	(47.1)	194	(26.8)	74	(49.3)		928	(36.3)

*Data are shown in median (IQR, Interquartile range) or frequencies and percentages, n (%); *Closest measure within two years at baseline; **Chronical kidney disease, Cancer, Diabetes, Cardiovascular event, Hypertension and Osteoporosis.*

During the period, 3735 treatment sequences were initiated in 3298 PLWH, ranging from 1182 on BIC/FTC/TAF to 194 on DTG/ABC/3TC. The main characteristics are (table 1):

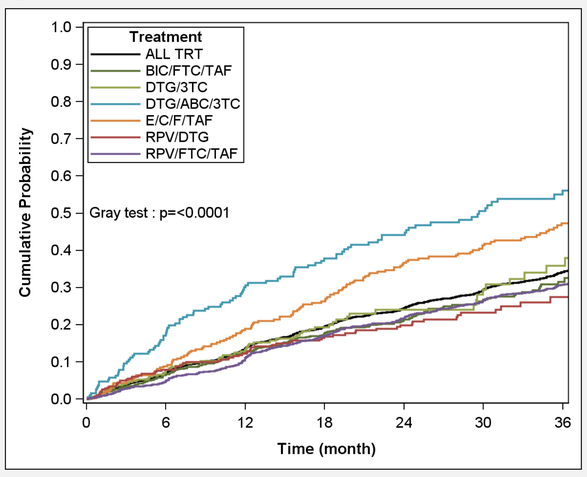
- Median age was 52.8 years and ranged significantly (p<0.05) from 50.5 years on E/C/F/TAF and DTG/RPV to 55.9 years DTG/RPV;
- Women represented 28,5% of PLWH, the difference between STRs treatments populations was not significant (p>0.05);
- MSM represented 44.6% of the study population and ranged significantly (p<0.05) from 40.2% on DTG/ABC/3TC to 49% on DTG/3TC
- Median BMI was 24.4, without any differences at the start of STR
- 13.2% were of sub-Saharan origin ranged significantly (p<0.05) from 8% on DTG/RPV to 16.2% on RPV/FTC/TAF.
- The median CD4 count was 703 cells/mm^3 [IQR: 510-924].
- Among PLWH on STRs, 36.3% had two or more comorbidities, with rates varying significantly (p<0.05) from 26.8% among those on RPV/FTC/TAF to 49.3% among those on DTG/ABC/3TC.

Figure 2. Evolution of median BMI between baseline and 18 month



- Between baseline and M18, median BMI increased, from 24.4 for all individuals at baseline to 25.0 for those still on treatment at M18 (figure 2).
- At M18, PLWH with RPV/FTC/TAF, DTG/ABC/3TC and DTG/3TC as STR have a higher BMI than the overall group, although the increase then BMI increase less than 1 point.

Figure 3. Risk curve of STRs discontinuation with patients censored at their last follow-up date



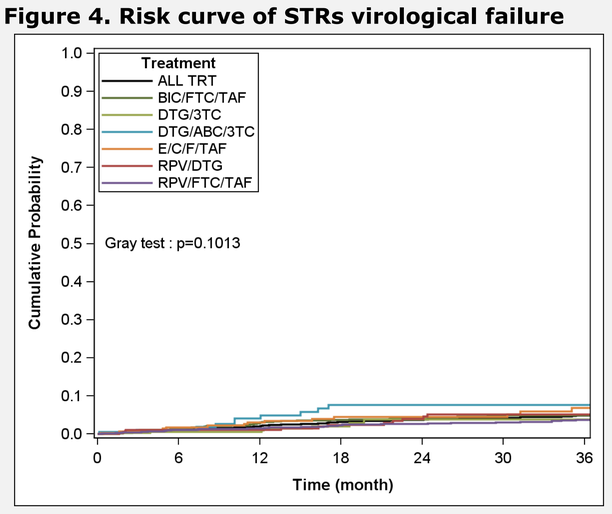
- The cumulative probability of STRs discontinuation was 19.5% [IQR: 18.2-20.9] at M18 (figure 3).
- The higher risk of STRs discontinuations at M18 were for E/C/F/TAF (26,3% [IQR: 21.3-31.6]) and DTG/ABC/3TC (37.9% [IQR: 30.7-45.0]).
- The rate of discontinuation of other STRs was approximately 18% at M18.

Table 2. Most frequents reasons of STRs discontinuation at M18

	BIC/FTC/TAF		DTG/3TC		E/C/F/TAF		RPV/DTG		RPV/FTC/TAF		DTG/ABC/3TC		p*	Total	
Characteristics	N=1182		N=492		N=307		N=413		N=1147		N=194			N=3735	
Switch at M18, n (%)													<0.0001		
Yes	175	(14.8)	63	(12.8)	74	(24.1)	57	(13.8)	184	(16.0)	68	(35.1)		621	(16.6)
Reason for Switch at M18, n (%)	175		63		74		57		184		68			621	
Any adverse events	62	(35.4)	20	(31.7)	16	(21.6)	21	(36.8)	59	(32.1)	22	(32.4)		200	(32.2)
Physician choice / drug reducing	31	(17.7)	20	(31.7)	21	(28.4)	13	(22.8)	40	(21.7)	12	(17.6)		137	(2.1)
Patient choice	30	(17.1)	6	(9.5)	4	(5.4)	7	(12.3)	20	(10.9)	8	(11.8)		75	(12.1)
Non-optimal treatment	18	(10.3)	8	(12.7)	25	(33.8)	7	(12.3)	33	(17.9)	19	(27.9)		110	(17.7)
Death	16	(9.1)	1	(1.6)	1	(1.4)	4	(7.0)	8	(4.3)	2	(2.9)		32	(5.2)
Virological failure	10	(5.7)	5	(7.9)	5	(6.8)	1	(1.8)	8	(4.3)	1	(1.5)		30	(4.8)
Pregnancy (or desire)	5	(2.9)	1	(1.6)	2	(2.7)	1	(1.8)	12	(6.5)	3	(4.4)		24	(3.9)
Other	3	(1.7)	2	(3.2)	0	(0.0)	3	(5.3)	4	(2.2)	1	(1.5)		13	(2.1)
Description of the reason: Any adverse events , n (%)	62		20		16		21		59		22			200	
Neurological event	16	(25.8)	5	(25.0)	3	(18.8)	6	(28.6)	14	(23.7)	7	(31.8)		51	(25.5)
Digestive event	10	(16.1)	3	(15.0)	8	(50.0)	2	(9.5)	15	(25.4)	6	(27.3)		44	(22.0)
General sign	14	(22.6)	4	(20.0)	2	(12.5)	5	(22.7)	8	(13.6)	2	(9.1)		35	(17.5)
Weight gain	9	(14.5)	1	(5.0)	0	(0.0)	2	(9.5)	2	(3.4)	2	(9.1)		16	(8.0)
Hypersensitivity reaction	5	(8.1)	3	(15.0)	0	(0.0)	2	(9.5)	4	(6.8)	1	(4.5)		15	(7.5)
Kidney event	3	(4.8)	3	(15.0)	1	(6.3)	2	(9.5)	1	(1.7)	1	(4.5)		11	(5.5)
Hepatic event	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	2	(3.4)	0	(0.0)		3	(1.5)
Others events	5	(8.1)	1	(5.0)	2	(12.6)	0	(0.0)	13	(22.1)	3	(13.6)		25	(12.5)
Outcome after STRs discontinuation, n (%)	175		63		74		57		184		68		<0.0001	621	
Other combination	88	(50.3)	36	(57.1)	16	(21.6)	19	(33.3)	97	(52.7)	21	(30.9)		277	(44.6)
One of the 6 study STRs	48	(27.4)	20	(31.7)	50	(67.6)	27	(47.4)	67	(36.4)	39	(57.4)		251	(40.4)
No subsequent treatment	23	(13.1)	6	(9.5)	7	(9.5)	7	(12.3)	12	(6.5)	6	(8.8)		61	(9.8)
Deceased	16	(9.1)	1	(1.6)	1	(1.4)	4	(7.0)	8	(4.3)	2	(2.9)		32	(5.2)

- By M18 (Table 2), 16.6% had switched STR treatment, ranged significantly (p<0.05) from 12.8% for DTG/3TC to 35.1% for DTG/ABC/3TC.
- The most common reason for discontinuation was « Any adverse events » in 32.2% including: neurological event (25.5%); digestive event (22%); general symptoms (17.5%); weight gain (8%).
- Among PLWH who stopped treatment, 40.4% switched to another STR, ranged significantly (p<0.05) from 27.4% for BIC/FTC/TAF to 67.6% for E/C/F/TAF.
- Among the PLWH who were not on treatment immediately after discontinuation, 34/61 (55.7%) were still untreated after one month.

Figure 4. Risk curve of STRs virological failure



- Overall, the cumulative probability of virological failure was 3.1% [IQR: 2.5-3.8] at M18 with no significant difference between STRs (figure 4),
- Among the 95 PLWH who experienced virological failure during the 18 month, 71.6% remained one the same STRs. Among of the 27/95 (28.4%) who change the treatment, 5 change for another study STRs (table 3).

Table 3. Description of the outcome of STRs treatment after virological failure at M18

	BIC/FTC/TAF		DTG/3TC		E/C/F/TAF		RPV/DTG		RPV/FTC/TAF		DTG/ABC/3TC		p*	Total	
VF, n (%)	35		7		11		7		25		10			95	
Discontinuation	9	(25.7)	4	(57.1)	5	(45.5)	1	(14.3)	7	(28.0)	1	(10.0)	0.2626	27	(28.4)
Outcome after STRs discontinuation, n (%)													0.1721		
No subsequent treatment	2	(22.2)	0	(0.0)	0	(0.0)	1	(100.0)	2	(28.6)	0	(0.0)		5	(18.5)
One of study's STRs	0	(0.0)	1	(25.0)	2	(40.0)	0	(0.0)	1	(14.3)	1	(100.0)		5	(18.5)
Other combination	7	(77.8)	3	(75.0)	3	(60.0)	0	(0.0)	4	(57.1)	0	(0.0)		17	(63.0)

Conclusion

- Despite a simplification approach with STRs, the rate of discontinuation of STRs reach 20% at M18
- This rate of discontinuation is mainly driven by adverse events, accounting for one third of causes of discontinuation and treatment optimization, mainly for the oldest STRs E/C/F/TAF and DTG/ABC/3TC.
- A moderate increase of BMI was observed for all STRs at M18
- Virologically-suppressed PLWH who switched to one of the STRs maintained a high level of virologic suppression (96.9%) at M18.

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