

Dettaglio abstract

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Title: Reasons for choosing DRV/cob/FTC/TAF in ART-naïve and ART-experienced patients: data from the Icona Cohort

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Treatment of naïve PLWH: current strategies and rapid start of ART

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Abstract

Background: Despite the preferential use of unboosted INSTI drugs, darunavir (DRV) is still recommended in all major guidelines and widely used. This study provides insight into the characteristics of People Living with HIV (PLWH) who started darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in a real-world setting.

Materials and Methods: Observational study using data from the multicentre Italian ICONA Cohort starting from January 2017. PLWH who started from ART-naïve D/C/F/TAF, 3TC/DTG, FTC/TAF/INSTI or FTC/TAF/RPV regimen or PLWH who switched from any other regimen to D/C/F/TAF were included, regardless of HIV-RNA and the type of regimen (single and multi-tablet). The objective was to evaluate predictors of starting D/C/F/TAF from ART-naïve vs several comparator groups (1. FTC/TAF/INSTI; 2. FTC/TAF/RPV; 3. 3TC/DTG) or switching to D/C/F/TAF for the first time from another non boosted-DRV (b-DRV) based regimen. Unadjusted and adjusted logistic regression models were constructed to identify factors associated with the probability of starting from naïve D/C/F/TAF vs. other considered regimens. In the ART-experienced group, a comparison between subjects with or without a b-DRV regimen before the switch was performed. Unadjusted and adjusted logistic regression models were fitted to identify factors associated with the switch to D/C/F/TAF without previous exposure to b-DRV.

Results: 2050 ART-naïve subjects were included, of which 289 (14%) started D/C/F/TAF, 158 FTC/TAF/RPV (7.7%), 238 3TC/DTG (11.6%) and finally 1365 FTC/TAF/INSTI (66.6%). Main patients' characteristics are shown in Table 1. Predictors of starting D/C/F/TAF over 2DR INSTI-based, FTC/TAF/INSTI-based or FTC/TAF/RPV are shown on Table 2; AIDS diagnosis at presentation, high HIV-RNA load and low CD4 count (<200 cells/mm³) are some of the most common independent predictors. Compared to FTC/TAF/RPV and 3TC/DTG the D/C/F/TAF had a higher probability of being started in a 'rapid-ART' timeframe. 685 PLWH switched for the first time to D/C/F/TAF, 34% in the STR formulation; 80% of subjects were male, median age was 47 years (37-54), 78% Italian, 42% heterosexual and 39% MSM. Median CD4 cell count was 568 cells/mm³ (358-793) and 20% had HIV-RNA >50 copies/ml at switch. 212 PLWH (31%) did not have b-DRV in the previous regimen. In the adjusted logistic regression model, independent predictors of switching to D/C/F/TAF from non b-DRV regimen were recent calendar year of switch, female sex, non-Italian, HIV-RNA > 50 copies/ml at switch, a higher number of previous virological failure and serum glucose > 100 mg/dL (Table 3).

Conclusions: The well-known potency and high genetic barrier of b-DRV make D/C/F/TAF one of the main choices for ART-start in advance naïve and highly viraemic patients. In patients switching from non b-DRV regimen, D/C/F/TAF is considered a valid option in subjects with a long history of ART, previous

virological failures, or current failure at switch.

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Table 1. Main patients' characteristics according to first ART regimen

	3TC/DTG		FTC/TAF/INSTI		FTC/TAF/DRV/cob		p-value	Total			
	N=238	11.6%	N=1365	66.6%	N=158	7.7%	N=289	14.1%	N=2050	100.0%	
Regimen, n(%)	238	100.00	0	0.00	0	0.00	0	0.00	238	11.61	
3TC/DTG	0	0.00	464	34.00	0	0.00	0	0.00	464	22.63	
FTC/TAF/BI	0	0.00	587	46.00	0	0.00	0	0.00	587	28.63	
FTC/TAF/DTG	0	0.00	315	23.10	0	0.00	0	0.00	315	15.37	
FTC/TAF/DRV/cob	0	0.00	0	0.00	158	100.00	0	0.00	158	7.71	
FTC/TAF/DRV/cob	0	0.00	0	0.00	0	0.00	289	100.00	289	14.10	
Single Tablet Regimen, n(%)	84	35.30	778	57.00	150	94.90	135	46.70	<0.001	1147	55.95
Italian, n(%)	169	71.01	1,009	73.92	116	73.42	209	72.32	0.789	1,503	73.32
Gender, Male, n(%)	210	88.24	1,146	83.93	116	73.42	243	84.08	0.001	1,715	83.66
Calendar Year of start, median(IQR)	2020	2019-2020	2019	2018-2020	2018	2018-2018	2019	2018-2019	<0.001	2019	2018-2020
Age, median (IQR)	38	29-48	41	32-51	37	30-47	41	33-48	0.002	40	31-50
Mode of HIV Transmission, n(%)	72	30.25	543	39.78	51	32.28	112	38.75	0.006	778	37.95
Heterosexual	15	6.30	80	5.86	13	8.23	18	6.23		126	6.15
IDU	135	56.72	652	47.77	81	51.27	124	42.91		992	48.39
MSM	16	6.72	90	6.59	13	8.23	35	12.11	0.041	53	2.59
Other/Unknown	0	0.00	41	3.00	7	4.43	5	1.73		53	2.59
HIV-1 RNA > 5 log copies/mL, n(%)	13	5.46	73	5.35	11	6.96	14	4.84	0.021	111	5.41
AIDS, Yes, n(%)	2	0.84	163	11.9	0	0.0	58	20.1	<0.001	223	10.9
CD4, cells/mm ³ , median (IQR)	483	344-702	302	99-504	546	438-697	200	74-387	<0.001	337	130-546
CD4 <200	11	4.62	513	37.58	1	0.63	144	49.83	<0.001	669	32.63
CD4 200-350	51	21.43	267.0	19.56	19	12.0	51.0	17.65		388.0	18.93
CD4 350-500	63	26.47	238.0	17.44	45	28.5	42.0	14.63		388.0	18.93
CD4 >500	113	47.48	347	25.42	93	48.86	52	17.99		605	29.51
HIV-RNA > 5 log copies/mL, median (IQR)	4.46	3.80-4.91	5.04	4.41-5.62	4.13	3.62-5.64	5.19	4.63-5.64	<0.001	4.89	4.26-5.52
HIV-RNA > 5 log copies/mL, n(%)	47	19.57	675	49.45	4	2.53	160	55.36	<0.001	866	42.22
Total Cholesterol, median (IQR)	164	145-192	157	135-183	165	139-192	155	129-185	<0.001	159	136-186
Triglycerides, median (IQR)	89	69-136	99	71-146	92	71-127	107	78-149	0.009	99	71-143
Serum Glucose, median (IQR)	85	79-92	86	79-94	85	78-93	86	78-93	0.518	86	79-94
eGFR, CKD-EPI formula, ml/min, median (IQR)	107.2	94.2-117.5	106.6	92.8-117.2	110.2	98.5-119.1	109.3	98.3-119.1	0.009	107.4	94.1-117.7
BMI, kg/m ² , median (IQR)	23.4	21.3-25.7	23	20.9-25.1	23.4	21.5-26.1	22.6	20.9-24.3	0.025	23.1	20.84
Obese, n(%)	14	5.88	39	2.86	1	0.63	4	1.38	<0.001	60	2.93
Diabetes diagnosis, n(%)	8	3.36	43	3.15	4	2.53	10	3.46	0.956	65	3.17
CVD diagnosis, n(%)	1	0.42	9	0.66	1	0.63	1	0.35	0.912	12	0.59
Hypertension, n(%)	18	7.56	106	7.77	17	10.76	36	5.54	0.26	157	7.66
Days from HIV diagnosis to ART start, median(IQR)	30	18-74	21	11-44	52	28-223	22	12-50	<0.001	24	13-52
<=14 days from diagnosis to start (rapid start), n(%)	34	14.29	490	35.90	15	9.49	101	34.95	<0.001	640	31.22

Table 2. OR and Adjusted OR of starting FTC/TAF/DRV/cob vs other regimen from fitting logistic regression models: A) VS dual 3TC/DTG, B) FTC/TAF/INSTI, C) FTC/TAF/DRV

	Starting 3TC/DTG		Starting FTC/TAF/DRV/cob over 3TC/DTG	
	OR	95%CI	AOR*	95%CI
Gender, Male (vs. Female)	0.70	0.49-1.02	0.71	0.51-1.01
Age, per 10 years older	1.31	1.04-1.61	0.816	0.51-1.24
Calendar year of ART start, per 1 month	0.70	0.67-0.73	0.70	0.67-0.73
Mode of HIV transmission				
Heterosexual	1.00		1.00	
IDU	0.77	0.37-1.63	0.66	0.31-1.42
MSM	0.99	0.40-2.47	0.807	0.33-2.05
Other/Unknown	1.41	0.73-2.72	0.312	0.14-1.42
Italian	1.07	0.91-1.26	0.94	0.80-1.12
Zone Italy				
Control	1.00		1.00	
North	1.09	0.74-1.59	0.677	0.40-1.13
South	0.95	0.73-1.23	0.805	0.51-1.26
University education	0.57	0.34-0.93	0.832	0.51-1.35
AIDS	0.63	0.55-0.72	0.605	0.48-0.76
HIV-RNA > 5 log copies/mL	1.04	1.4-7.48	<0.005	2.34-124.06
CD4, cells/mm ³				
>500	1.00		1.00	
350-500	1.45	0.87-2.41	0.554	0.37-0.82
200-350	2.17	1.11-4.24	0.808	0.48-1.34
<200	28.45	14.30-57.03	<0.001	15.16-28.07
Total Cholesterol >200 mg/dL	0.60	0.37-0.99	0.844	0.57-1.29
eGFR > 60 ml/min	0.60	0.40-0.90	0.959	0.56-1.61
BMI, kg/m ²	<18.5		0.58	0.36-0.97
18.5-24.9	1.58	0.83-3.08	0.84	0.51-1.41
≥25	0.56	0.33-0.97	0.88	0.51-1.41
<=14 Days from HIV diagnosis	1.22	2.02-6.90	<0.001	1.47-115.66
	Starting FTC/TAF/DRV/cob over FTC/TAF/INSTI		Starting FTC/TAF/DRV/cob over FTC/TAF/DRV	
	OR	95%CI	AOR*	95%CI
Calendar year of ART start, per 1 month	0.69	0.70-0.69	<0.001	0.67-0.71
Zone Italy				
Control	1.00		1.00	
North	0.42	0.31-0.58	<0.001	0.44-0.52
South	1.78	1.28-2.47	<0.001	1.84-2.14
AIDS	1.85	1.13-3.06	<0.001	1.81-1.94
HIV-RNA > 5 log copies/mL	1.27	0.89-1.84	0.568	0.79-1.31
CD4, cells/mm ³				
>500	1.00		1.00	
350-500	1.18	0.76-1.81	0.465	1.24-0.81
200-350	1.27	0.84-1.94	0.355	1.09-1.71
<200	1.87	1.13-3.05	<0.001	1.82-1.98
eGFR > 60 ml/min	0.60	0.40-0.90	0.807	0.48-1.34
BMI, kg/m ²	<18.5		0.38	0.19-0.76
18.5-24.9	0.60	0.30-1.20	0.584	0.33-1.0
≥25	0.38	0.19-0.76	0.065	0.27-0.81
<=14 Days from HIV diagnosis	0.60	0.30-1.20	0.584	0.33-1.0
	Starting FTC/TAF/DRV/cob over FTC/TAF/DRV		Starting FTC/TAF/DRV/cob over FTC/TAF/DRV	
	OR	95%CI	AOR*	95%CI
Gender, Male (vs. Female)	1.91	1.19-3.07	0.807	1.06-1.05-0.05
Calendar year of ART start, per 1 month	1.85	1.42-2.39	<0.001	1.81-1.29-1.54
Zone Italy				
Control	1.00		1.00	
North	0.78	0.51-1.22	0.28	0.28-0.26
South	2.86	1.63-5.00	<0.001	3.75-1.74-0.02
HIV-RNA, per 1 log copies higher	47.75	17.33-132.34	<0.001	1.87-1.63-1.1
CD4, cells/mm ³				
>500	1.00		1.00	
350-500	1.87	0.97-3.67	0.063	1.21-0.65-2.25
200-350	4.80	2.07-8.98	<0.001	3.19-1.53-0.66
<200	37.67	19.18-70.64	<0.001	18.03-10.19-3.05-8
BMI, kg/m ²				
18.5-24.9	1.00		1.00	
<18.5	0.92	0.45-1.8	0.82	0.44-0.91-0.44
≥25	0.40	0.16-0.94	0.04	0.40-0.27
<=14 Days from HIV diagnosis	0.12	7.85-9.19	<0.001	1.19-1.12-0.12

Table 3. OR and Adjusted OR of switching to FTC/TAF/DRV/cob without boosted-DRV use in the previous regimen by fitting logistic regression models

	OR	95%CI	p	AOR*	95%CI	p
Gender, Female (vs. Male)	1.72	1.17-2.53	0.005	1.80	1.06-3.06	0.029
Calendar year of cART start, per 1 month	2.54	2.11-3.06	<0.001	2.47	2.02-3.02	<0.001
Mode of HIV transmission						
Heterosexual	1.00			1.00		
IDU	1.83	1.11-3.01	0.017	1.43	0.74-2.77	0.293
MSM	0.94	0.65-1.35	0.723	1.47	0.90-2.39	0.127
Other/Unknown	1.11	0.56-2.20	0.767	1.25	0.58-2.71	0.575
Non-Italian	2.18	1.50-3.17	<0.001	1.62	1.02-2.60	0.041
Not Employed/Invalid	1.96	1.26-3.05	0.003	1.61	0.92-2.79	0.094
HIV-RNA > 50 copies/mL	2.97	2.03-4.35	<0.001	2.18	1.35-3.51	0.001
CD4, cells/mm ³						
>500	1.00			1.00		
350-500	0.78	0.49-1.25	0.304	0.84	0.49-1.44	0.529
200-350	0.79	0.48-1.30	0.354	0.63	0.34-1.16	0.137
<200	2.42	1.41-4.16	0.001	1.52	0.77-3.01	0.224
Serum Glucose > 100 mg/dL	1.88	1.25-2.82	0.003	1.81	1.12-2.93	0.016
Number of previous VF* before switch to FTC,TAF ,DRV,cob						
0	1.00			1.00		
1	1.67	0.73-3.79	0.222	1.07	0.40-2.82	0.896
>1	1.98	1.25-3.14	0.004	1.80	1.01-3.21	0.045

*Adjusted for all the factors showed in Table