PE 2/52

Virological outcomes of first line regimens in women living with HIV from Icona cohort: comparison with clinical trials data

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BACKGROUND AND AIMS

Women living with HIV (WLWH) are under-represented in RCT, and few studies are specifically designed. The aim of this analysis was to verify in a real-life setting the efficacy of newer cART regimens in WLWH and to compare the virological efficacy of regimens for whom WLWH-specific RCT are available (Waves[1] and ARIA[2]).

STUDY DESIGN AND METHODS

STUDY POPULATION

Naïve WLWH enrolled in Icona from 2006 starting a ATV/r-, DTG-, EVG/c-, DRV/r or DRV/c-, RAL-, RPV-based regimens regardless of backbone and with at least 1 follow-up HIVRNA were included.

OUTCOMES

Primary endpoint was treatment failure (TF) (confirmed HIV-RNA>200 c/mL after 24 weeks or discontinuation for any reason but simplification). Secondary endpoints: 1) first line discontinuation for any reason; 2) first line discontinuation for toxicity; 3) virological failure; 4) virological success at week 48 [Modified FDA Snapshot Algorithm]) for regimens mimicking WLWH-RCT.

STATISTICAL ANALYSIS

Cox regression model was used to estimate the hazard risk (HR) of various outcome according to different cART regimens, after adjusting for main confounders (AIDS diagnosis, Italian nationality, HCV Ab status, CD4 and HIV RNA at enrolment, NRTI backbone (TDF/FTC, TAF/FTC, ABV/3TC).

RESULTS

Table 1. General characteristics of total study population and according to third drug of ARV regimen

	Overall N=1048	ATV/b N=258	DGV N=166	EVG N=115	DRV/b N=219	RAL N=71	RPV N=219	
Age, median (IQR)	39 (31-48)	36 (30-44)	45 (33-55)	39 (32-50)	39 (31-47)	44 (32-52)	38 (29-49)	<0.001
Mode of HIV infection, n(%)								
heterosexual	885 (84.5%)	215 (83.3%)	139 (83.7%)	99 (86.1%)	186 (84.9%)	62 (87.3%)	184 (84.0%)	0.297
IVDU	91 (8.7%)	27 (10.5%)	11 (6.6%)	10 (8.7%)	21 (9.6%)	1 (1.4%)	21 (9.6%)	
other/unknown	72 (6.9%)	16 (6.2%)	16 (9.6%)	6 (5.2%)	12 (5.5%)	8 (11.3%)	14 (6.4%)	
Nationality, n(%)								
Italian	576 (55.0%)	132 (51.2%)	87 (52.4%)	59 (51.3%)	124 (56.6%)	40 (56.3%)	134 (61.2%)	<0.001
not Italian	402 (38.3%)	125 (48.5%)	58 (34.9%)	39 (33.9%)	88 (40.2%)	24 (33.8%)	68 (31.0%)	
missing	70 (6.7%)	1 (0.4%)	21 (12.7%)	17 (14.8%)	7 (3.2%)	7 (9.9%)	17 (7.8%)	
AIDS diagnosis, n(%)	128 (12.2%)	26 (10.1%)	25 (15.1%)	16 (13.9%)	45 (20.6%)	9 (12.7%)	7 (3.2%)	<0.001
HCVAb, n(%)								
negative	822 (78.4%)	198 (76.7%)	128 (77.1%)	91 (79.1%)	174 (79.5%)	59 (83.1%)	172 (78.5%)	0.153
positive	102 (9.7%)	35 (13.6%)	9 (5.4%)	9 (7.8%)	21 (9.6%)	6 (8.5%)	22 (10.0%)	
missing	124 (11.8%)	25 (9.7%)	29 (17.5%)	15 (13.0%)	24 (11.0%)	6 (8.5%)	25 (11.4%)	
HBsAg, n(%)								
negative	879 (83.9%)	224 (86.6%)	131 (78.9%)	92 (80.0%)	187 (85.4%)	63 (88.7%)	182 (83.1%)	0.386
positive	36 (3.4 %)	9 (3.5%)	5 (3.0%)	6 (5.2%)	5 (2.3%)	2 (2.8%)	9 (4.1%)	
missing	133 (12.7%)	25 (9.7%)	30 (18.1%)	17 (14.8%)	27 (12.3%)	6 (8.5%)	28 (12.8%)	
CD4, cell/mmc, n(%)								
0-200	324 (30.9%)	80 (31.0%)	64 (38.6%)	43 (37.4%)	94 (42.9%)	26 (36.6%)	17 (7.8%)	<0.001
201-350	253 (24.1%)	85 (33.0%)	30 (18.1%)	24 (20.9%)	59 (26.9%)	14 (19.7%)	41 (18.7%)	
351+	447 (42.7%)	88 (34.1%)	66 (39.8%)	46 (40.0%)	60 (27.4%)	29 (40.8%)	158 (72.2%)	
missing	24 (2.3%)	5 (1.9%)	6 (3.6%)	2 (1.7%)	6 (2.7%)	2 (2.8%)	3 (1.4%)	
HIVRNA, copies/mL n(%)								
<100.000	690 (65.8%)	156 (60.5%)	103 (62.0%)	74 (64.4%)	107 (48.9%)	41 (57.8%)	209 (95.4%)	<0.001
>=100.000	328 (31.3%)	96 (37.2%)	57 (34.3%)	40 (34.8%)	103 (47.0%)	27 (38.0%)	5 (2.3%)	
missing	30 (2.9%)	6 (2.3%)	6 (3.6%)	1 (0.9%)	9 (4.1%)	3 (4.2%)	5 (2.3%)	
NRTI backbone, n(%)								
TDF/FTC	814 (77.7%)	219 (84.9%)	64 (38.6%)	95 (82.6%)	176 (80.4%)	58 (81.7%)	202 (92.2%)	<0.001
TAF/FTC	35 (3.3%)	0	5 (3.0%)	20 (17.4%)	3 (1.4%)	1 (1.4%)	6 (2.7%)	
ABC/3TC	199 (3.3%)	39 (15.1%)	97 (58.4%)	0	40 (18.3%)	12 (16.9%)	11 (5.0%)	

Table 2. Proportions of patients with HIV RNA<50 using FDA snapshot, on the subgroup of 404 WLWH starting regimens mimicking Waves[1] and ARIA[2] trials.

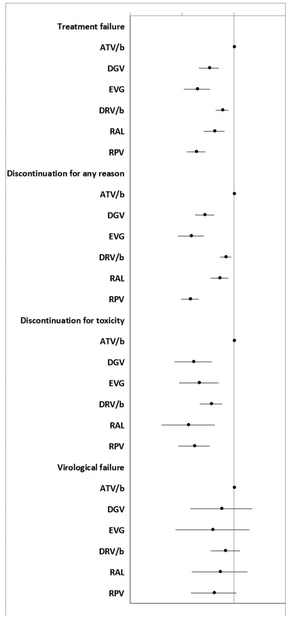
NRTI backbone	ATV/r N=211 (TAF/FTC or TDF/FTC)	DGV N=87 (ABC+3TC)	EVG N=106 (TAF/FTC or TDF/FTC)	TOT N=404
HIVRNA<50 copie/mL	107 (50.7%)	65 (74.7%)	84 (79.2%)	256 (63.4%)
HIVRNA>=50 copie/mL	36 (17.1%)	6 (6.9%)	7 (6.6%)	49 (12.1%)
Pts who changed any regimen component for failure before w48	4 (1.9%)	1 (1.1%)	0 (0%)	5 (1.2%)
Pts who changed any regimen component for toxicity before w48	33 (15.6%)	4 (4.6%)	5 (4.7%)	42 (10.4%)
Pts with no data in windows:				
-on study but missing data in windows	10 (4.7%)	3 (3.4%)	8 (7.5%)	21 (5.2%)
-discontinued regimen for reason other than failure/toxicity before w48	21 (10.0%)	8 (9.2%)	2 (1.9%)	31 (7.7%)

A subgroup of 404 women starting regimens analogous to those of WLWH enrolled in Waves an ARIA trials were selected.
The proportion of patients with HIVRNA<50 and other outcomes defined by FDA snapshot algoritm[3] were calculated in table 2 and compared with trial results.

WAVES trial: 48 weeks virological success in EVG arm 87%, in ATV/r 81%
ARIA trial: 48 weeks virological success in DGV arm 82%, in ATV/r 71%

Figure 1. Hazard ratio of primary and secondary outcomes according to third drug of the regimen by means of 4 separate Cox models.

After adjustment for AIDS diagnosis, nationality, CD4 cell count, plasma HIV-RNA, HCV-Ab status, NRTI backbone and calendar year of cART initiation, women on ATV/r showed higher risk of TF. The only other factor independently associated with higher risk of TF was AIDS (HR 1.58, 95%CI 1.13-2.20, p=0.007).
As regarding secondary outcomes, WLWH on ATV/r were associated with higher probability of discontinuation for any reason and discontinuation for toxicity.



	HR	95%CI	
Treatment failure			
ATV/b	1.00		
DGV	0.33	0.21	0.52
EVG	0.19	0.11	0.35
DRV/b	0.59	0.45	0.78
RAL	0.42	0.26	0.66
RPV	0.19	0.12	0.28
Discontinuation for any reason			
ATV/b	1.00		
DGV	0.27	0.18	0.42
EVG	0.15	0.08	0.27
DRV/b	0.70	0.54	0.89
RAL	0.52	0.35	0.78
RPV	0.14	0.10	0.21
Discontinuation for toxicity			
ATV/b	1.00		
DGV	0.16	0.07	0.38
EVG	0.21	0.09	0.51
DRV/b	0.36	0.22	0.59
RAL	0.13	0.04	0.43
RPV	0.17	0.08	0.34
Virological failure			
ATV/b	1.00		
DGV	0.58	0.15	2.28
EVG	0.39	0.07	2.01
DRV/b	0.68	0.35	1.32
RAL	0.53	0.16	1.83
RPV	0.41	0.15	1.11

CONCLUSIONS

In a real-world cohort of WLWH, treatment failure is still an issue, particularly in case of PI/r based regimens. Results from clinical practice are far from those obtained in trials and suggest the need for focused intervention on adherence and vulnerability support in this population.

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