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Outcomes of antiretrovirals used as the third drug in subgroups of treatment naïve individuals living with HIV

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Background

Although outcomes of ART have been evaluated in randomized controlled trials, experiences from subpopulations defined by age, CD4 count or viral load (VL) in heterogenous real-world settings are limited.

RESPOND aimed to compare shorter term (12 months) virologic and immunologic outcomes and longer-term clinical events of AIDS/death in ART-naïve persons starting ART in RESPOND with either an INSTI, PI/b or NNRTI regimen in a-priori defined relevant subgroups defined by age, CD4 count, severe immunosuppression (AIDS or CD4<200/mm^3) and VL.

Methods

- Logistic regression compared virologic and immunologic outcomes at 12±3 months after starting ART with an INSTI, contemporary NNRTI or PI/b with 2 nucleos(t)ides after 1/1/2012
- Composite treatment outcome [cTO] defined success as VL <200 copies/mL with no regimen change, AIDS or death. Immunologic success was defined as a CD4 >750 cells/mm^3 or 33% increase where baseline CD4 >500 cells/mm^3
- Poisson regression compared AIDS/death ≥14 days after starting ART
- Interactions between ART class and age, CD4 count, VL were determined for each endpoint.

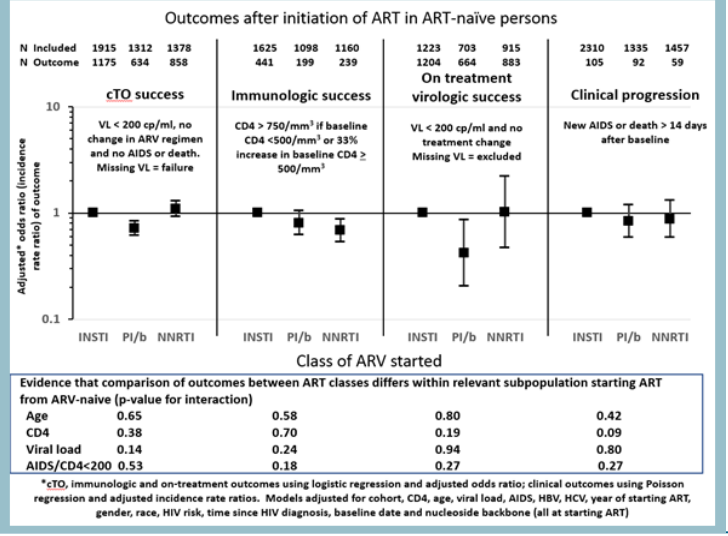
Results

Of 5102 ART-naïve persons in RESPOND, 45.3% started INSTIs, 26.2% PI/b and 28.6% NNRTIs (Table). The most commonly used nucleoside backbone was TDF/FTC (n=3655; 71.7%) and ABC/3TC (n=905; 17.7%). Those starting PI/b regimens were more likely to be female, have a higher VL and lower CD4 count nadir. Those starting INSTIs had started ART more recently.

Characteristics of included study participants

		INSTI		PI/b		NNRTI	
		N	%	N	%	N	%
All		2310	45.3	1335	26.2	1457	28.6
Gender	Male	1937	83.9	1022	76.6	1211	83.1
	Female	373	16.1	313	23.4	246	16.9
Ethnic Origin	White	1592	68.9	927	69.4	1057	72.5
	Other	330	14.3	232	17.4	235	16.1
	Unknown	388	16.8	176	13.2	165	11.3
HIV Acquisition risk	MSM	1379	59.7	642	48.1	825	56.6
	IDU	99	4.3	107	8.0	96	6.6
	Heterosexual	643	27.8	490	36.7	465	31.9
	Other/Unknown	189	8.2	96	7.2	71	4.9
Nucleos(t)ide Backbone	TDF/FTC	1300	56.3	1075	80.5	1280	87.9
	TAF/FTC	388	16.8	12	0.9	39	2.7
	ABC/LAM	606	26.2	217	16.3	82	5.6
	Other	16	0.7	31	2.3	56	3.8
HIV viral load	<=100000	1383	59.9	750	56.2	1078	74.0
	>100000	927	40.1	585	43.8	379	26.0
CD4	<=350/mm^3	1111	48.1	814	61.0	614	42.1
	>350/mm^3	1199	51.9	521	39.0	843	57.9
Severe Immunosuppression*	No	1615	69.9	825	61.8	1178	80.9
	Yes	695	30.1	510	38.2	279	19.1
Age	<=40	1283	55.5	753	56.4	827	56.8
	41-50	585	25.3	367	27.5	407	27.9
	>50	442	19.1	215	16.1	223	15.3
Baseline	mm/yy	1/16	1/15–1/17	8/13	8/12–8/14	2/14	1/13–5/15

*CD4 < 200/mm^3 or AIDS



Evidence that comparison of outcomes between ART classes differs within relevant subpopulation starting ART from ARV-naive (p-value for interaction)

Age	0.65	0.58	0.80	0.42
CD4	0.38	0.70	0.19	0.09
Viral load	0.14	0.24	0.94	0.80
AIDS/CD4<200	0.53	0.18	0.27	0.27

*cTO, immunologic and on-treatment outcomes using logistic regression and adjusted odds ratio; clinical outcomes using Poisson regression and adjusted incidence rate ratios. Models adjusted for cohort, CD4, age, viral load, AIDS, HBV, HCV, year of starting ART, gender, race, HIV risk, time since HIV diagnosis, baseline date and nucleoside backbone (all at starting ART)

Results ctd

Outcomes are summarized in the Figure

- 2667 (57.9%; 95% CI 56.0–59.8%) achieved cTO success; 1175 on INSTIs (61.4%; 95% CI 58.6–64.1%), 634 (48.3%; 95% CI 44.4–52.4%) on PI/b and 858 on NNRTIs (62.3%; 95% CI 59.0–65.5%).
- 879 (22.6%; 95% CI 21.3–24.0%) achieved immunologic success; 441 on INSTIs (27.1%; 95% CI 25.0–29.3%), 199 (18.1%; 95% CI 15.8–20.4%) on PI/b and 239 on NNRTIs (20.6%; 95% CI 18.3–22.9%)
- 256 persons had a new AIDS diagnosis or died > 14 days after initiation of ART during 15082 PYFU; incidence rate 17.0/1000 PYFU (95% CI 14.9–19.1). The incidence was highest for INSTIs (21.2; 95% CI 17.2 -25.3), followed by PI/b (18.1; 95% CI 14.4–21.8) and lowest in NNRTI (11.7; 95% CI 8.7–14.7).
- cTO, immunologic success and clinical failure were completely consistent across age groups (≤40, 40-50 and >50 years), CD4 count at starting ART (≤350 versus >350 cells/mm^3), VL at starting ART (≤100,000 versus >100,000 copies/mL) or in those with/without severe immunosuppression - all interactions were non-significant (p>0.05).

Limitations and Strengths

- The main limitations are confounding by indication and not being adequately powered to look at the impact of individual ARVs
- The major strengths were the heterogeneity, the inclusion of routine clinic populations, and inclusion of clinical events as an endpoint

Conclusions

Virologic, immunologic and clinical outcomes in ART-naive participants were similar for different ART classes irrespective of age, immune suppression or VL at ART initiation. While confounding by indication cannot be excluded, this provides reassuring evidence that such subpopulations will equally benefit from ART, regardless of ART class

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