First Antiviral Regimen and Modification Patterns in People Who Recently Acquired HIV

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BACKGROUND

- Modern antiretroviral therapy (ART) is highly efficacious; yet, modification is still required due to adverse effects, simplification, safety and/or loss of virological control.
- Stage of HIV infection (heterogeneous in most studies to date) and the ART regimen can influence time to first treatment modification.
- **Objective**: To examine time to first ART modification (including predictors and modification type) in people diagnosed within 12 months of HIV acquisition in post 2015 era.

METHODS

- **CASCADE study:** A multinational study of cohorts from France, the Netherlands, Spain, Sweden, Greece, Canada and the UK.
- All participants have well estimated dates of HIV-1 seroconversion (SC) with a HIV-1 test window ≤12 months or other laboratory evidence of seroconversion.

Inclusion criteria

- ART initiation on 1/1/2015 or later,
- ART regimens of first ART: PI, NNRTI, first- (raltegravir, elvitegravir) or second- (dolutegravir, bictegravir) generation INSTI regimen.
- Maintenance of first ART: at least for 1 month.

Definitions

Treatment modification: change of ≥1 drug in the regimen

Treatment interruption: cessation of all drugs for ≥15 days

Statistical analysis

- Cause-specific hazard models for:
  - time-to-treatment modification (competing event: treatment interruption).
  - type of treatment modification by initial ART class (competing events: each possible subsequent regimen).
- Adjusting for probable HIV exposure route, region of origin, acute infection (lab evidence or HIV negative-to-positive interval ≤30 days), time from SC to ART start, and stratifying by calendar year of ART initiation.

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- Overall, rate of ART modification was 54.8% over a median time of 32 months.
- Second-generation INSTIs demonstrated the greatest durability, with most treatment modifications involving changes to the backbone.
-Compared with MSM, women exhibited lower modification rates when ART was initiated with a PI, but switched regimens more rapidly when starting with other drug classes.

RESULTS

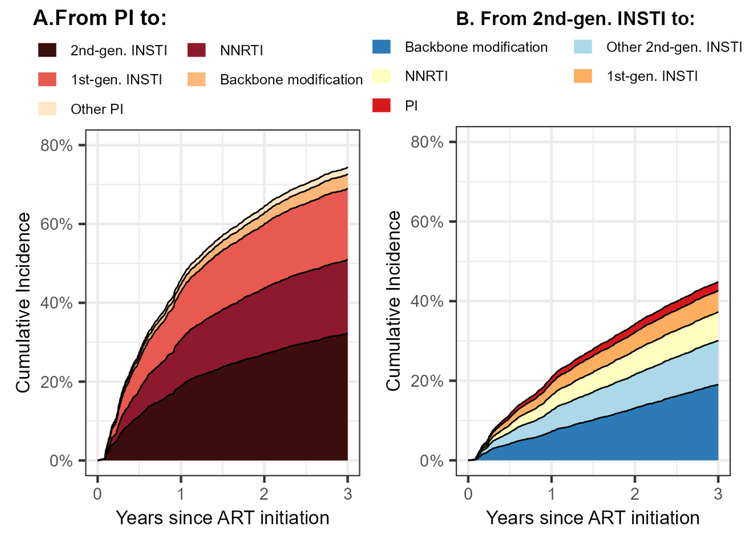
- 6,225 individuals were included in the analysis; 80% men who have sex with men (MSM), 10.5% women who have sex with men (WSM), 69.8% from Europe/North America, and 9.3% from Sub-Saharan Africa. 63.9% started ART within 6 months from SC.
- 3,135 (50.3%) started ART with a second-generation INSTI, 15.9% with a PI-based regimen.
- 3,411 (54.8%) modified their first ART regimen; median time = 32 months; 262 (4.2%) interrupted it.
- Hazard for treatment modification was lower for WSM compared to MSM when starting with a PI regimen (HR=0.82; p=0.049), but higher when starting with NNRTI (HR=1.33; p=0.029), first- (HR=1.38; p=0.006) and second-generation INSTI (HR=1.27; p=0.022) (Table).

Table. Factors associated with the hazard for treatment modification: Results from multivariable cause-specific hazard regression.

Variable	HR	95% CI	P
Age at ART initiation (ref: ≤29)			
30-39	1.09	1-1.18	0.046
30-49	1.04	0.95-1.15	0.384
≥50	1.14	1.03-1.28	0.016
Region of origin (ref: Europe/N.America)			
Sub-Saharan Africa	0.95	0.83-1.09	0.492
Lat.America/Caribbean	1.03	0.92-1.15	0.649
Other	0.96	0.85-1.08	0.519
Probable exposure route (ref: MSM) x ART class			
PI:WSM (n=177)	0.82	0.66-1	0.049
NNRTI:WSM (n=127)	1.33	1.03-1.72	0.029
1st-gen. INSTI:WSM (n=126)	1.38	1.10-1.74	0.006
2nd-gen. INSTI: WSM (n=223)	1.27	1.03-1..55	0.022
PI:MSW (n=97)	0.90	0.70-1.16	0.408
NNRTI:MSW (n=69)	0.99	0.69-1.42	0.967
1st-gen. INSTI:MSW (n=100)	1.10	0.86-1.41	0.456
2nd-gen. INSTI: MSW (n=251)	0.93	0.75-1.15	0.491
PI:PWID (n=7)	0.68	0.25-1.83	0.444
NNRTI:PWID (n=9)	0.52	0.19-1.39	0.194
1st-gen. INSTI:PWID (n=15)	0.77	0.37-1.63	0.499
2nd-gen. INSTI: PWID (n=41)	0.56	0.30-1.05	0.073
Diagnosed during acute infection (ref: No)			
Yes	1.18	1.09-1.27	<0.001
Time from SC to ART start (ref:<3 months)			
3-6 months	0.75	0.69-0.82	<0.001
>6 months	0.62	0.57-0.67	<0.001

- Shorter time from SC to ART initiation was associated with higher hazard for treatment modification, while region of origin showed no association (Table).
- Over 60% of those starting a PI regimen switched class within 3 years (mainly to 2nd-gen. INSTIs; Figure A), while 2nd–gen. INSTIs showed the lowest modification rates (mostly in the backbone; Figure B).

Figure. Cumulative incidence of ART modification among people starting ART with PI (A.) or second-generation INSTI (B.)



CONCLUSIONS

- Individuals started on second-generation INSTIs were less likely to experience ART modification.
- WSM were more likely to switch from 2nd-generation INSTIs compared to people of other routes of exposure. This could be attributed to concerns around pregnancy.
- Investigation of the specific reasons for modification will provide valuable insights.

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PLAIN LANGUAGE SUMMARY

We analyzed data from 6,225 people across 8 countries, who were diagnosed with HIV soon after acquiring it, and who started HIV treatment after 2015. We found that around 6 in every 10 people changed their treatment within a few years, usually to newer drugs. People starting treatment with dolutegravir or bictegravir based regimens were the least likely to change treatment. However, women were more likely than men to switch from these regimens, possibly because of pregnancy-related concerns.