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Transmitted and Acquired Integrase Strand Transfer Inhibitor (INSTI) Resistance Mutations in a Prospective Cohort of Thai People Living with Acute HIV

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BACKGROUND

- Data on Transmitted and Acquired Integrase Strand Transfer Inhibitor (INSTI) drug resistance mutations (TDRM and ADRM) in Thailand are limited.
- TDRM is optimally detected during acute HIV infection (AHI), before significant viral mutations occur, making the RV254/SEARCH010 AHI cohort a valuable resource for TDRM monitoring.
- This study assessed the prevalence of INSTI TDRM and ADRM in a longitudinal early-treated AHI cohort in Thailand.

METHODS

- The RV254/SEARCH010 cohort enrolls participants who are diagnosed and initiated treatment during acute HIV infection and follows participants for up to 20 years.
- HIV genotyping was done in RV254/SEARCH010 to identify TDRM at enrolment (before ART initiation) and ADRM in participants experiencing virologic failure (VF).

RV254 Enrolment
HIV genotyping
Transmitted DRM
→
DTG-based regimen initiation
→→
Virologic failure
HIV genotyping
Acquired DRM

- DTG-based regimens and integrase gene sequencing were introduced in SEARCH010/RV254 in 2017, with results analyzed using the Stanford University HIV Drug Resistance Database.

RESULTS

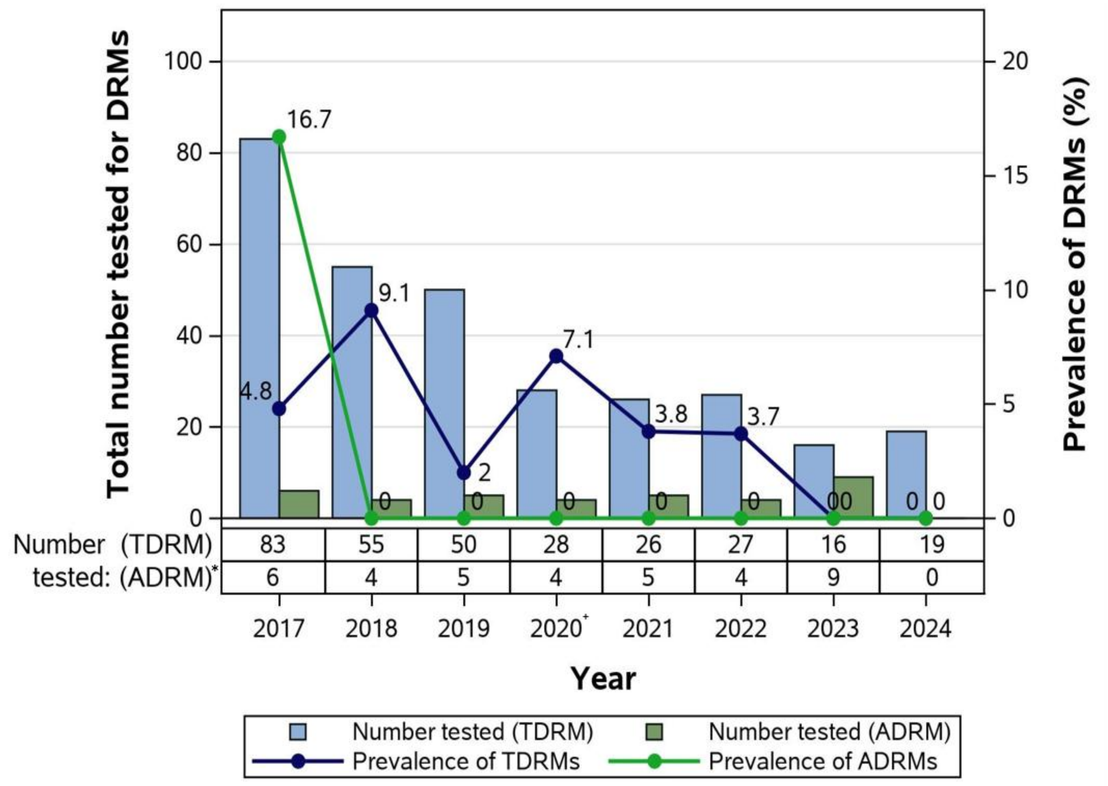
- INSTI TDRM data prior to ART initiation were available for 304 participants while sequencing was also available for 32 participants who experienced VF after earlier control on DTG-based ART.

TABLE 1. Participants with INSTI transmitted drug resistance screening before initiation of ART and participants who experienced virologic failure while on DTG-based regimen

Demographic characteristics	Participants with AHI with TDR screening (N=304)	Participants treated since AHI with ADR testing after VF (N=32)
Age (years), median (IQR)	27.0 (23.0, 32.0)	24.5 (22.5, 28.0)
Male, n (%)	299 (98.4%)	31 (96.9%)
Duration since HIV exposure (days), median (IQR) (N=171)	20.0 (13.0, 27.0)	
Sexual partners in past 30 days, median (IQR) (N=303)	2 (1,3)	
Drug use in past 30 days	59 (19.4%)	
Fiebig staging, n (%)		
1	45 (14.8%)	
2	65 (21.4%)	
3	151 (49.7%)	
4	40 (13.2%)	
5	1 (0.3%)	
6	2 (0.7%)	
HIV RNA (log10 copies/ml), median (IQR)	6.1 (5.0, 6.8)	4.6 (4.0, 5.1)
CD4 cell count (cells/mm3), median (IQR)	342.5 (247.0, 456.0)	584.0 (462.0, 655.0)
HIV subtype, n (%)		
CRF01_AE	191 (62.8%)	25 (78.1%)
CRF01_AE/B	95 (31.3%)	5 (15.6%)
B	3 (1.0%)	1 (3.1%)
CRF01_AE/C		1 (3.1%)
Non-Typable	4 (1.3%)	
Missing	11 (3.6%)	
Exposure to HIV Post-exposure prophylaxis (PEP), n (%)	21 (6.9%)	
Exposure to HIV Pre-exposure prophylaxis (PrEP), n (%)	23 (7.6%)	
Duration between initiating ART until VF (years), median (IQR)		4.6 (2.1, 6.4)
Duration of DTG at genotypic testing (years), median (IQR)		2.8 (1.6, 4.6)

Abbreviations: INSTI, integrase strand transfer inhibitor; ART, antiretroviral therapy; AHI, acute HIV infection; TDR: transmitted drug resistance; ADR, acquired drug resistance; VF, virologic failure

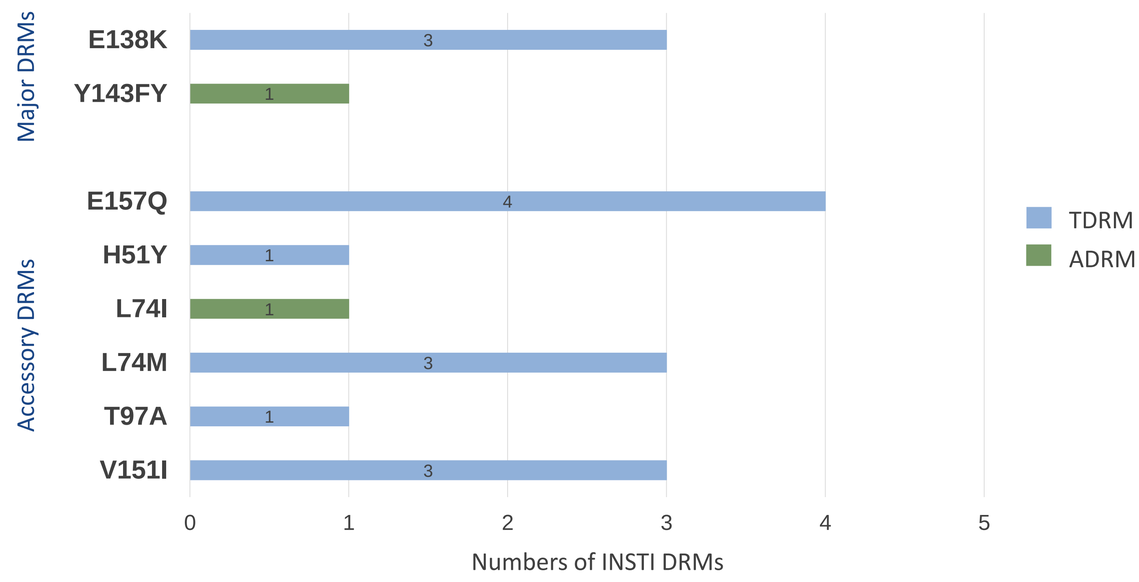
FIGURE 1. Prevalence of INSTI drug resistance mutations by year



* Virologic failure occurred in 32 participants at 37 distinct instances
+ National roll out of DTG-based regimen

Abbreviations: INSTI, integrase strand transfer inhibitor; DRM, drug resistance mutation; TDRM, transmitted drug resistance mutation; ADRM, acquired drug resistance mutation

FIGURE 2. Patterns of INSTI drug resistance mutations



Abbreviations: INSTI, integrase strand transfer inhibitor; DRM, drug resistance mutation; TDRM, transmitted drug resistance mutation; ADRM, acquired drug resistance mutation

CONCLUSION

- INSTI TDRM decreased over time in this AHI cohort, reflecting low current community transmission of INSTI resistance.
- INSTI ADRM was rare after VF, reflecting high barrier to resistance of DTG-based regimens, which may also be favorable for clinical trials incorporating analytic treatment interruptions and supporting ART switching without drug-resistance testing.
- The majority of the observed INSTI mutations were minor and would not affect the use of INSTIs for treatment or prevention.

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DISCLAIMER

The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army, the Department of Defense, the National Institutes of Health, the Department of Health and Human Services, or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. The investigators have adhered to the policies for protection of human subjects as prescribed in AR-70-25.

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