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Impact of Resistance to Antiretroviral Therapy Among Veterans with Human Immunodeficiency Virus

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OBJECTIVE

- Antiretroviral drug resistance remains a challenge complicating treatment and adversely affecting clinical outcomes for people living with HIV (PWH).[1,2]
- The objective of this study was to evaluate clinical outcomes associated with resistance to antiretroviral therapy (ART) among PWH.

METHODS

- This national retrospective cohort study was conducted using data from the United States Department of Veterans Affairs. The Veterans Affairs Informatics and Computing Infrastructure (VINCI) database was utilized to obtain individual-level information of structured claims data on demographics, medical claims, and pharmacy dispensation.
- Study cohorts were created by resistance testing results: 1) No resistance associated mutations (RAM) cohort, 2) those with any RAMs and 3) those with ≥1 major RAMs. Resistance cohorts had ≥1 documented RAM in integrase, protease or reverse transcriptase genes as defined by the International Antiviral Society-USA.[3]

RESULTS

- 7,746 veterans had interpretable resistance tests. Among all veterans with RAMs, PI resistance was most common, whereas among veterans with major RAMS, NNRTI and NRTI RAMS were most common (Table 1)

Table 1. Baseline demographics and clinical characteristics

	No RAMs N=1,875	Any RAMs N=5,871	Major RAMs N=1,406
Mean age (SD)	49.9 (12.64)	50.3 (11.4)	50.9 (10.1)
Sex: Male, N (%)	1811 (96.6%)	5688 (96.9%)	1373 (97.7%)
Mean year of resistance test (SD)	2013 (5.2)	2012 (5.1)	2009 (4.1)
Charlson comorbidity Index	0.89 (1.61)	0.87 (1.47)	0.84 (1.36)
Mean time from first HIV diagnosis, years (SD)	5.1 (5.9)	5.4 (5.3)	5.8 (4.2)
M184V/I mutation, N (%)*	-	538 (9.2%)	538 (38.3%)
Resistance Class, N (%)**			
INSTI	-	97 (1.6%)	<11†
NRTI	-	388 (6.6)	385 (27.4%)
NNRTI	-	493 (8.4%)	470 (33.4%)
PI	-	2475 (42.1%)	208 (14.8%)
Multiclass	-	355 (6.1%)	339 (24.1%)

*Counts and percentages are based on PWH who tested positive for M184V/I; those who did not receive testing were assumed to be negative for M184V/I
**Counts and percentages are based on the number of PWH with categorizable resistance tests; if a chart noted that resistance was detected without noting the RAM or class, this was classified as "Any RAM" since it could not be confirmed as major.
INSTI: integrase inhibitor, NRTI: nucleoside reverse transcriptase inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor, PI: protease inhibitor
†Numbers less than 11 were not reportable due to patient confidentiality

RESULTS

- Median CD4 counts were higher among those without RAMs and opportunistic infections (OI) were lower versus those with RAMs (Table 2)

Table 2. CD4 count at index and opportunistic infections

	No RAMs N=1,875	Any RAMs N=5,871	Major RAMs N=1,406
ART at baseline, N (%)	656 (34.9%)	1806 (30.7%)*	475 (33.8%)
Median (IQR) CD4 count within 60 days +/- index	358 (362)	294 (343)*	285 (333)*
Number missing	882	2970	
CD4<200 N (%)	261 (26.3%)	1032 (35.6%)*	272 (36.4%)*
OI during follow-up			
Any OI, N (%)	71 (3.8%)	305 (5.2%)*	72 (5.1%)
Pneumocystosis, N (%)	43 (2.3%)	188 (3.2%)	42 (3.0%)
Mycobacteria, N (%)	27 (1.4%)	84 (1.4%)	26 (1.9%)
Cryptococcal meningitis, N (%)	<11†	41 (0.7%)	<11†
Cytomegalovirus, N (%)	<11†	32 (0.6%)	<11†

*p<0.05 †Numbers less than 11 were not reportable due to patient confidentiality

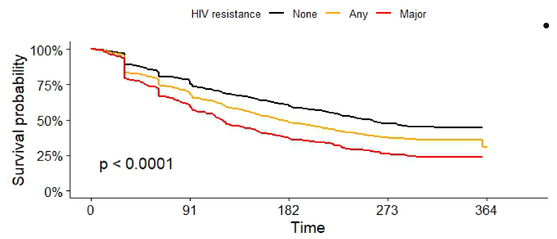
- Hospitalizations were more frequent in both the major RAM and any RAM cohorts versus no resistance (p<0.001 for both)
- Among veterans who switched or added therapies after the index resistance test, those with major NNRTI resistance were most likely to add a PI
- Those with major NRTI resistance were equally likely to add an NNRTI or INSTI
- Those with PI or multi-class resistance generally added a PI (Table 2)

Table 3. Treatment switch/add-on among those with major RAMs

		Resistance type			
		NNRTI N=41	NRTI N=51	PI N=160	Multiclass N=88
Drug class added	NNRTI	<11†	20 (39.2%)	39 (24.4%)	<11†
	INSTI	14 (34.2%)	20 (39.2%)	57 (35.6%)	27 (30.7%)
	PI	30 (73.2%)	16 (31.4%)	87 (54.4%)	71 (80.7%)

†Numbers less than 11 were not reportable due to patient confidentiality

Figure. ART Persistence among PWH without ART at index



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- For PWH not taking ART at index who then initiated ART, those with any RAMs and especially major RAMs were more likely to discontinue ART (Figure)
- Results were similar for PWH taking ART at index, with the No-RAMs group having the highest persistence and the Major RAM group have the lowest persistence

CONCLUSIONS AND LIMITATIONS

- These results are descriptive and not adjusted for potential confounders; additionally, all veterans received resistance testing and it is unknown how results would compare to those not receiving resistance tests
- HIV drug resistance was associated with a more complex patient profile in clinical and therapy outcomes, with veterans harboring major RAMs exhibiting lower CD4 counts and reduced ART persistence
- Interventions to prevent resistance may impact long-term health outcomes, reduce patient complexity, and preserve immunologic status and ART options
- Preventing resistance development may reduce the burden of HIV to health systems, payors, and patients

Acknowledgements

This study was funded by Gilead Sciences. The content of this poster is solely the responsibility of the authors and does not necessarily represent the official views of the US Department of Veterans Affairs, nor does mention of trade names, commercial products, or organizations imply endorsement by the US government. This research represents original research conducted, in part, using data from the Department of Veterans Affairs and is the result of work supported with resources and the use of facilities at the Dorn Research Institute, Columbia VA Health Care System, Columbia, South Carolina.

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