

# Integrase inhibitors and virological failure: a cohort analysis

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Montejano Rocio; De Miguel, Rosa; Bernardino, Jose I; Perez-Valero, Ignacio; Montes, M Luisa; Valencia, Eulalia; Martin-Carbonero, Luz; Moreno, Victoria; Gonzalez-Garcia, Juan; Arribas, Jose R  
Hospital La Paz HIV Unit Madrid Spain

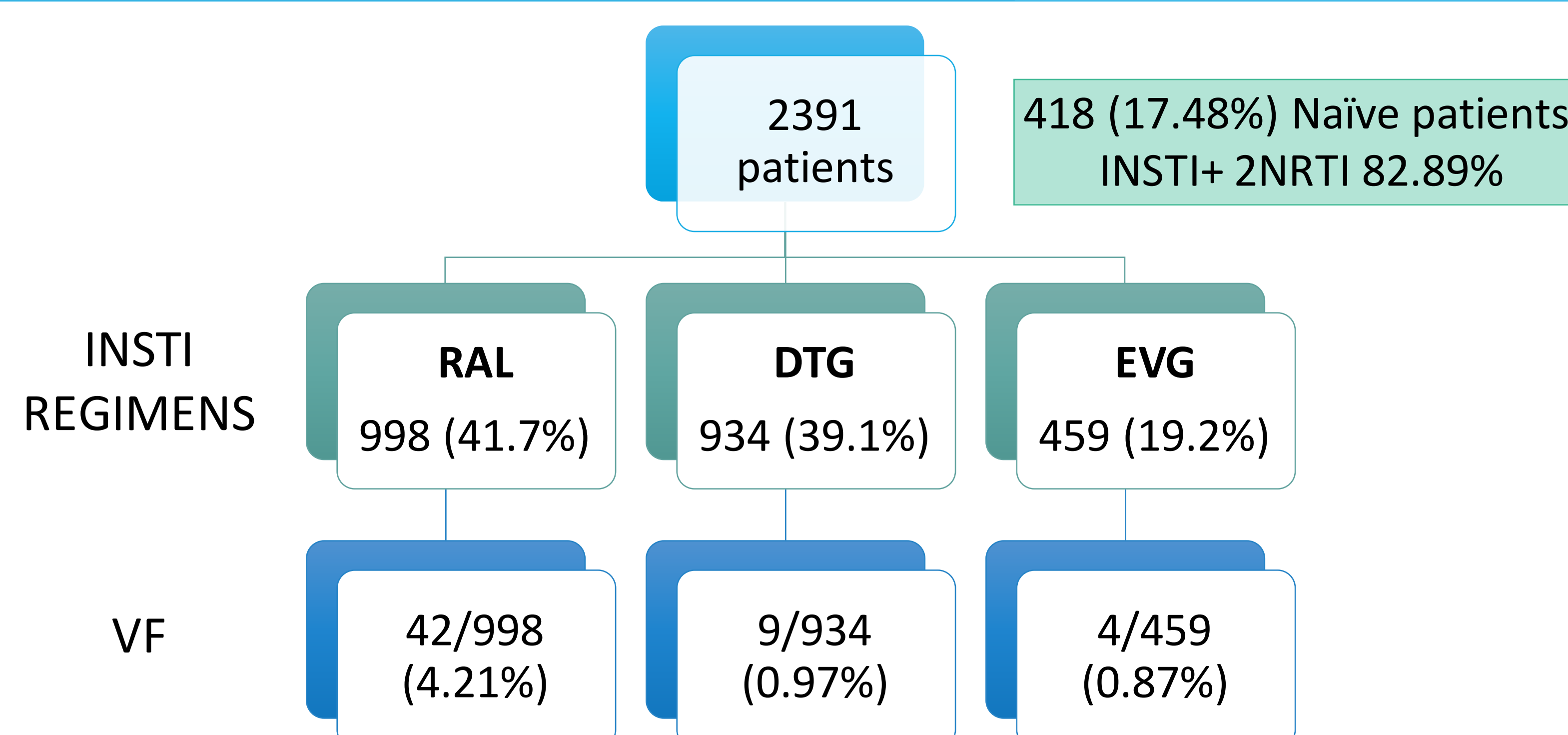
## BACKGROUND

- ART Guidelines recommend INSTI [in combination with 2 NRTIs] as the preferred initial regimen for HIV treatment, owing to their great efficacy and tolerability.
- Virologic failure (VF) in clinical trials of naïve-infected patients is less than 2%.
- However, data of VF in PLWHIV with INSTI-based regimens (either naïve or experienced) in real life setting are still scarce.
- We analysed a large cohort with current or previous INSTI-based ART, aiming to describe VF in these patients and identify frequency and characteristics of VF.

## PATIENTS AND METHODS

- Retrospective cohort study .
- Observational analysis (June 2006- June 2018) of 3960 outpatients with active follow-up attending Hospital La Paz (Madrid).
- Inclusion criteria: patients receiving INSTI based regimens with ART stable for at least 6 months.
- VF was defined as 2 consecutive viral loads (VL)> 200 copies/mL in patients with a prior VL <50 copies/mL.
- Patients participating in clinical trials were excluded.
- Relevant clinical information was obtained from our database.

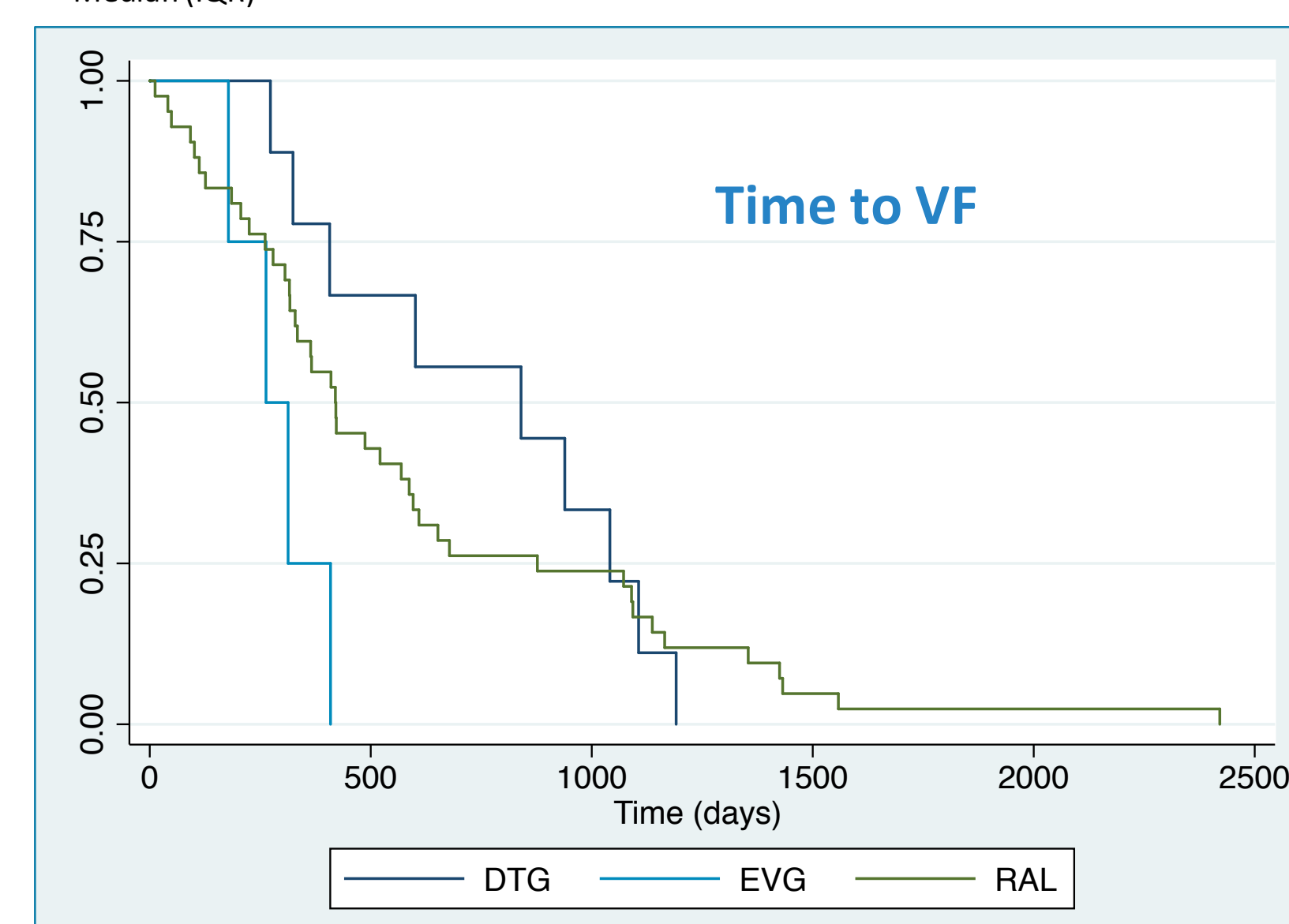
## RESULTS



### VF characteristics by INSTI drug

	RAL	DTG	EVG	p
N	42	9	4	<0.001
Sex, Male	27 (64.2%)	7 (77.7%)	4 (100%)	0.278
Age, years	43 (IQR 38-50)	48 (IQR 33-53)	53 (IQR 49-57)	0.084
Race, Caucasian	36 (85.7%)	7 (77.8%)	3 (75%)	0.750
HIV transmission				
- Sexual	18 (42.6%)	4 (44.4%)	3 (75%)	0.670
- IVDU	15 (35.7%)	4 (44.4%)	1 (25%)	
- Other	9 (21.4%)	1 (11.1%)	-	
Time with HIV, years	16 (IQR 11-19)	13 (IQR 8-21)	10 (IQR 5-15)	0.552
CD4 Nadir, cells/ml	97 (IQR 36-180)	50 (IQR 10-170)	125 (IQR 90-208)	0.432
AIDS stage	25 (59.5%)	7 (77.7%)	2 (50%)	0.522
Initial VL<50 cop/ml	19 (45.2%)	2 (22.2%)	2 (50%)	0.421
Initial CD4 count, cells/ml	201 (IQR 37-412)	154 (IQR 79-256)	-	0.191
VL at failure, log	3.5 (IQR 2.5-4.3)	3.2 (IQR 2.7-4.7)	2.9 (IQR 2.7-3.2)	0.107
Low level viremia at VF	13 (30.5%)	2 (22.2%)	1 (25%)	0.705
Time to VF, days	420 (261-877)	840 (IQR 407-1041)	288 (IQR 220-361)	0.083

\* Median (IQR)



10 patients presented 2 VF  
**ALL treated with RAL**

### Situation after VF

58.2% currently have CV<50 copies/mL  
median CD4 347 cels/mm<sup>3</sup> (180-638)  
76.4 %maintain treatment with INSTI  
- 19 with 2 NRTIs  
- 15 with Nuke-sparing regimens  
The most used INSTI: DTG, in 32/42 patients

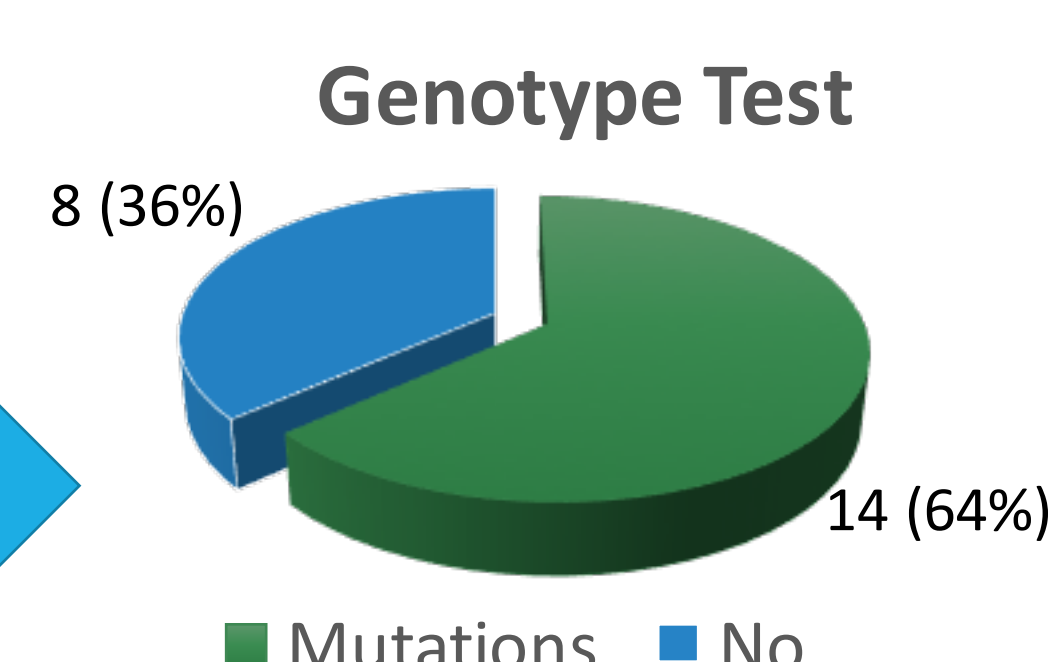
### Baseline characteristics of patients on INSTI ART

	ALL	No VF	VF	p
N	2391	2336	55	
Sex, Male	1869 (78.1%)	1831 (78.3%)	38 (69.1%)	0.099
Age, years	47 (IQR 39-52)	47 (IQR 39-52)	45 (IQR 38-51)	0.497
Race, Caucasian	2075 (89.2%)	2029 (89.6%)	46 (83.6%)	0.219
HIV transmission				
- Sexual	1490 (62.3%)	1465 (62.7%)	25 (45.5%)	<b>0.030</b>
- IVDU	626 (26.2%)	606 (26%)	20 (36.3%)	
- Other	275 (11.5%)	265 (11.3%)	10 (18.2%)	
Time with HIV, years	13 (IQR 5-21)	13 (IQR 5-21)	15 (IQR 10-19)	0.092
AIDS, Y/N	1165 (48.7%)	1127 (48.2%)	38 (69.1%)	<b>0.002</b>
CD4 Nadir, cells/ml	206 (IQR 92-327)	208 (IQR 93-329)	97 (IQR 20-180)	<b>0.001</b>
ART experienced	1973 (82.5%)	1922 (82.2%)	51 (92.7%)	<b>0.044</b>

\* Median (IQR)

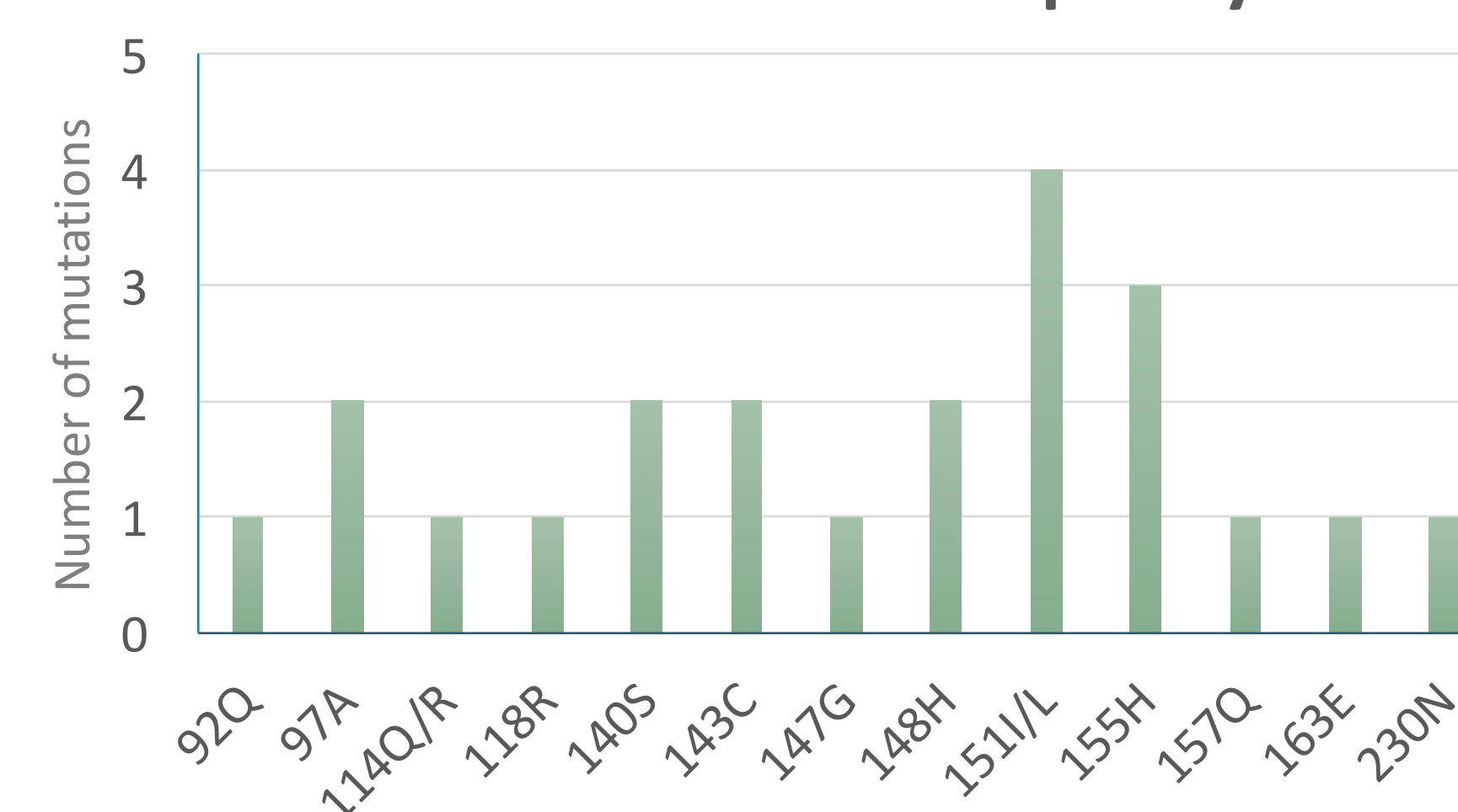
### Resistance mutations genotype

22/55 patients (40%)



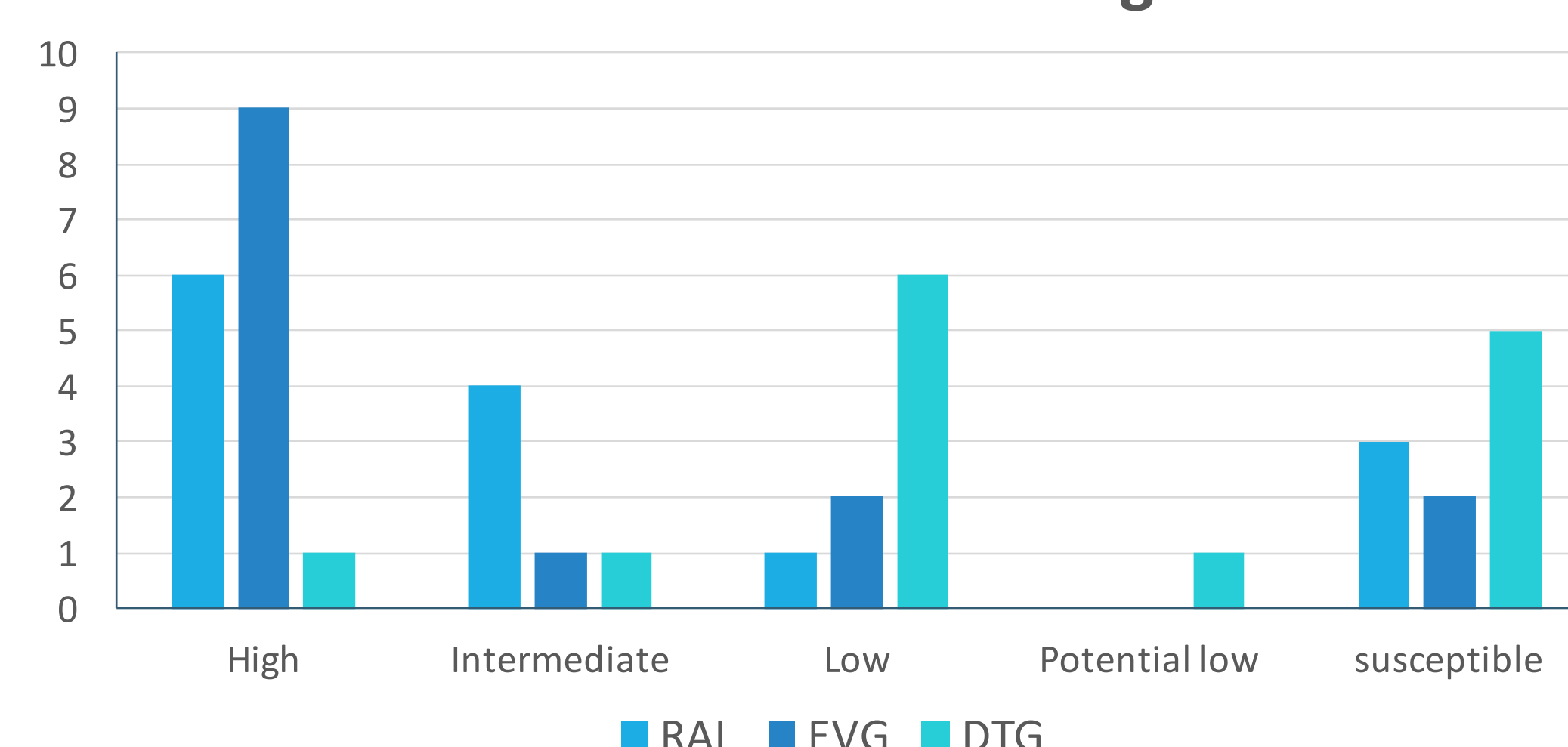
Number of mutations:  
- #1 mutation 42.8%  
- #2 mutations 50%

### INSTI mutations frequency



Mutations more frequently found:  
- 151I/L in 4/14 patients (28.6%)  
- 155H in 3/13 patients (21%)

### Patients with INSTI resistance according to Stanford database algorithm®



## CONCLUSIONS

- In our retrospective analysis, VF in INSTI-based treatments was infrequent in both naïve and experienced.
- After VF, the majority continued treatment with INSTI and currently more than half have undetectable VL.

### REFERENCES

- [http://gesida-seimc.org/wp-content/uploads/2018/01/gesida\\_TAR\\_adultos\\_v3-1.pdf](http://gesida-seimc.org/wp-content/uploads/2018/01/gesida_TAR_adultos_v3-1.pdf).
- [http://www.eacsociety.org/files/guidelines\\_9.0-english.pdf](http://www.eacsociety.org/files/guidelines_9.0-english.pdf)
- <https://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>