Dolutegravir plus Ritonavir-Boosted Darunavir in Highly cART-Experienced Subjects

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Background

- Dolutegravir (DTG) plus ritonavir-boosted darunavir (DRV/r) provides potency and a high genetic barrier toward HIV-1 resistance, and may fit for easy salvage regimens or simplification of complex regimens.
- The purpose of this work is to show the results of this regimen in clinical practice.

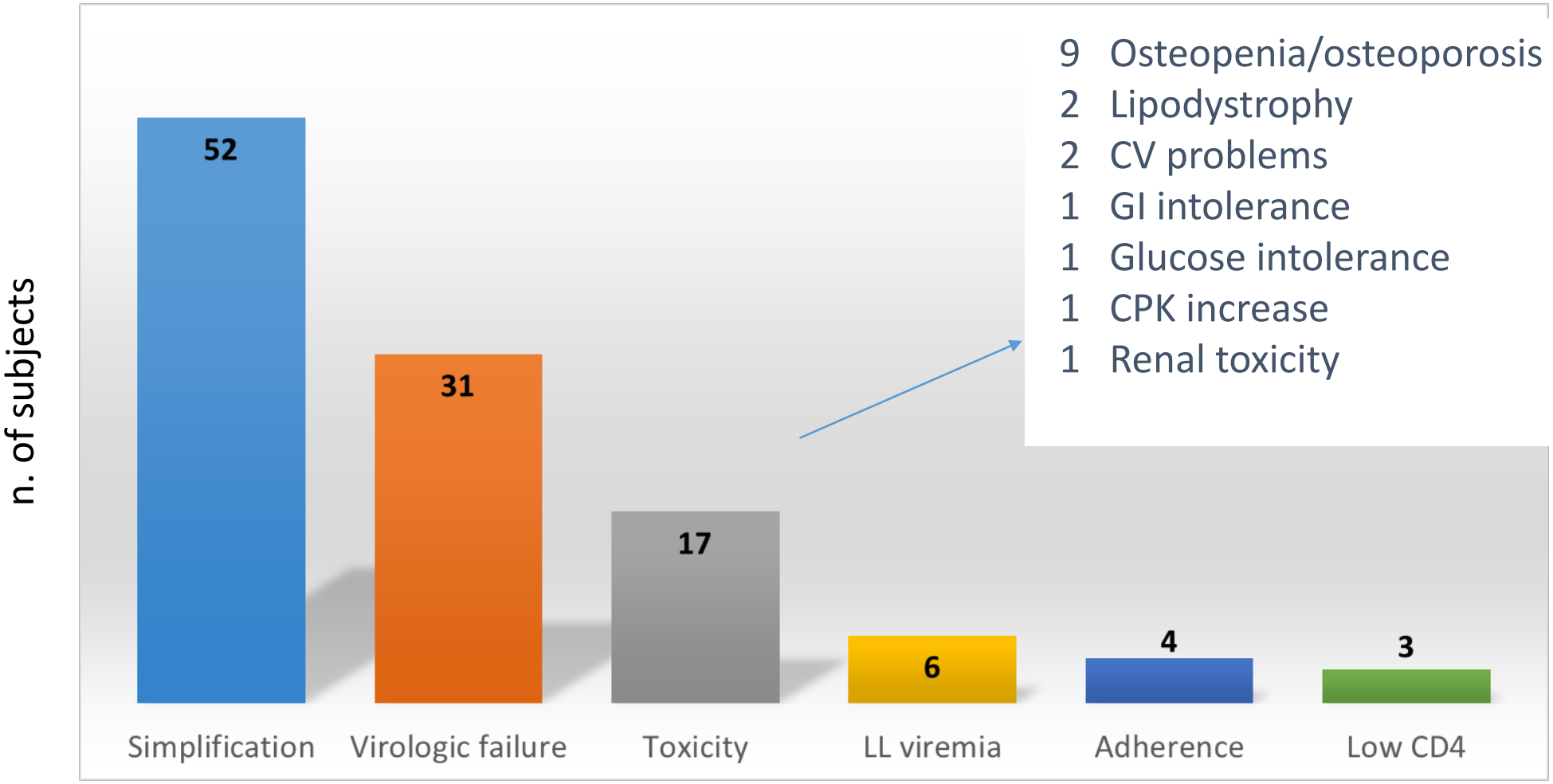
Methods

- All experienced HIV-1 infected subjects treated with DTG plus DRV/r in eleven centers in Italy were included between March 2014 and September 2015 in an observational cohort named Tivista (Tivicay plus Prezista Observational Cohort).
- CD4 cell counts, HIV-RNA and creatinine values were collected at baseline, at weeks 4, 12, 24 and 48.
- Patients were stratified by the baseline viral load into three groups: more than 50 copies per mL, less than 50 copies per mL but quantifiable HIV-RNA, and no virus detected (NVD).

Baseline patient demographics, 113 subjects

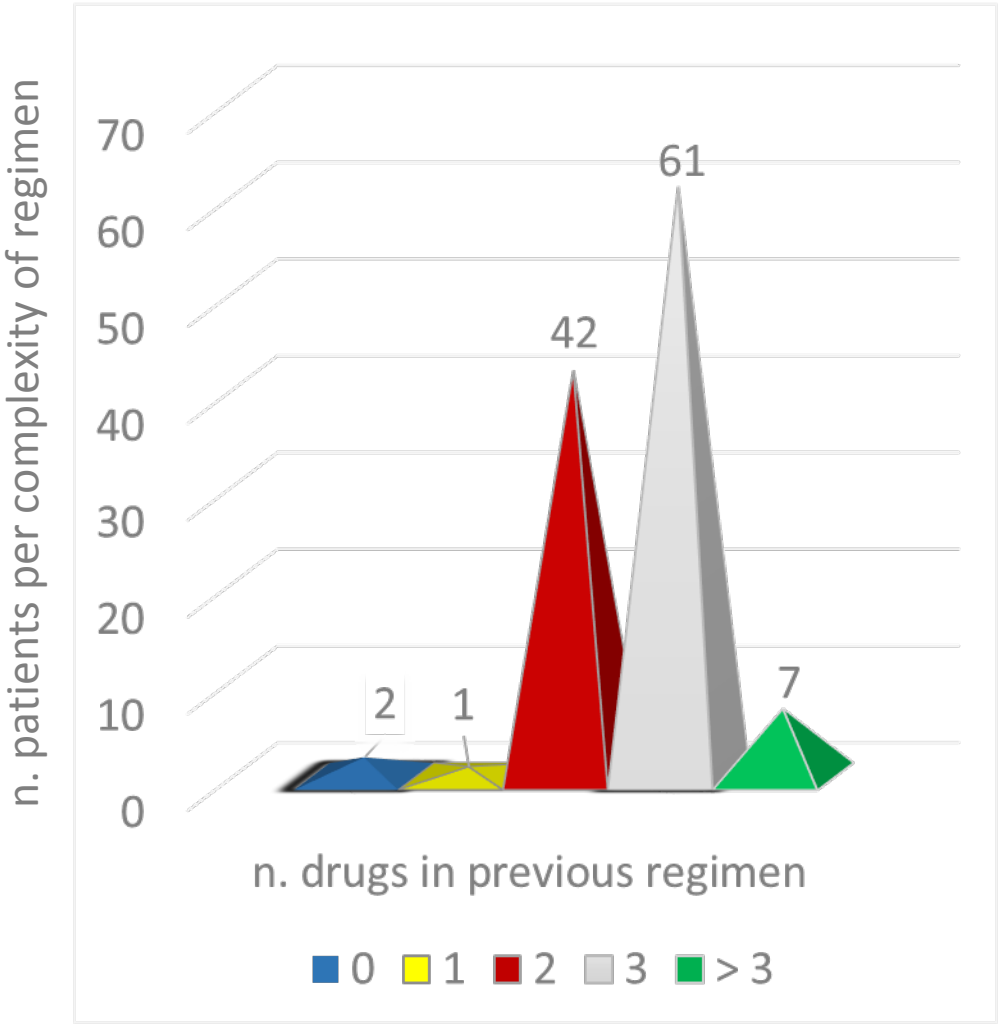
	Number (%)	Median (range)
Females/males	30/83 (26.5-73.5)	
Age, years		51 (24-82)
Non-caucasians	11 (9.7)	
CD4+ cell count (cells/µL)		632 (17-1693)
HIV-RNA, Log_{10} (copies/mL):		
• NVD	42 (37.3)	
• <50 quantifiable	23 (20.3)	
• >50	49 (43.4)	
Risk of transmission:		
• Sexual transmission	79 (69.9)	
• IDU	32 (28.3)	
• Other	2 (1.8)	
At least 1 failure in previous regimens	93 (82.3)	
Follow-up (weeks)		44 (24-234)

Reasons to switch

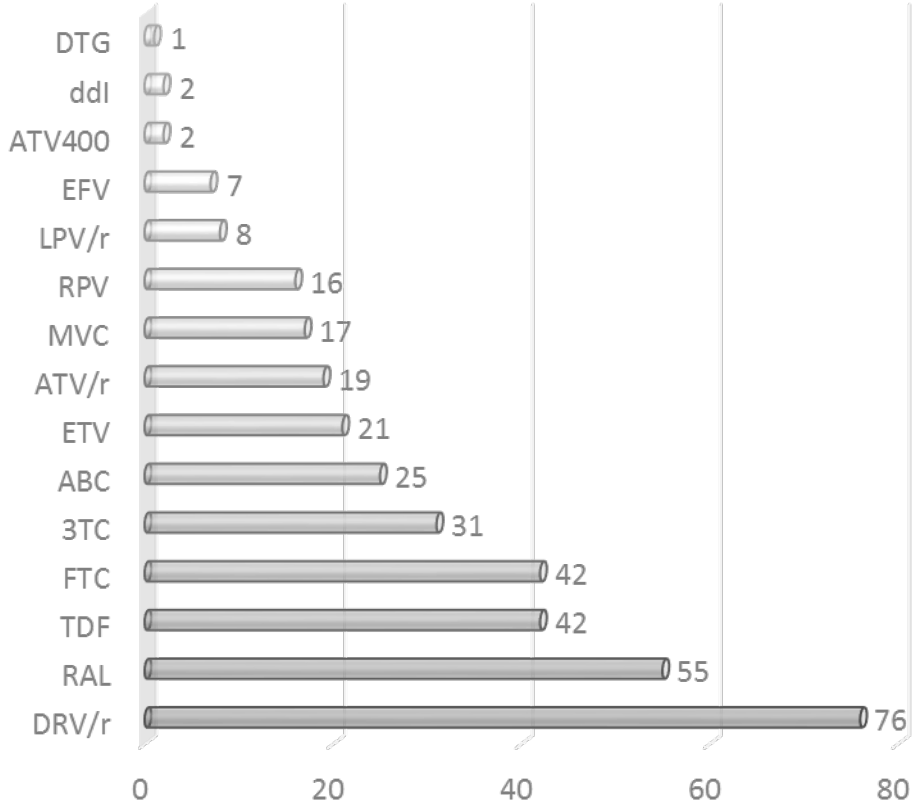


Patients' baseline disposition towards antiretrovirals

Complexity of the former regimen

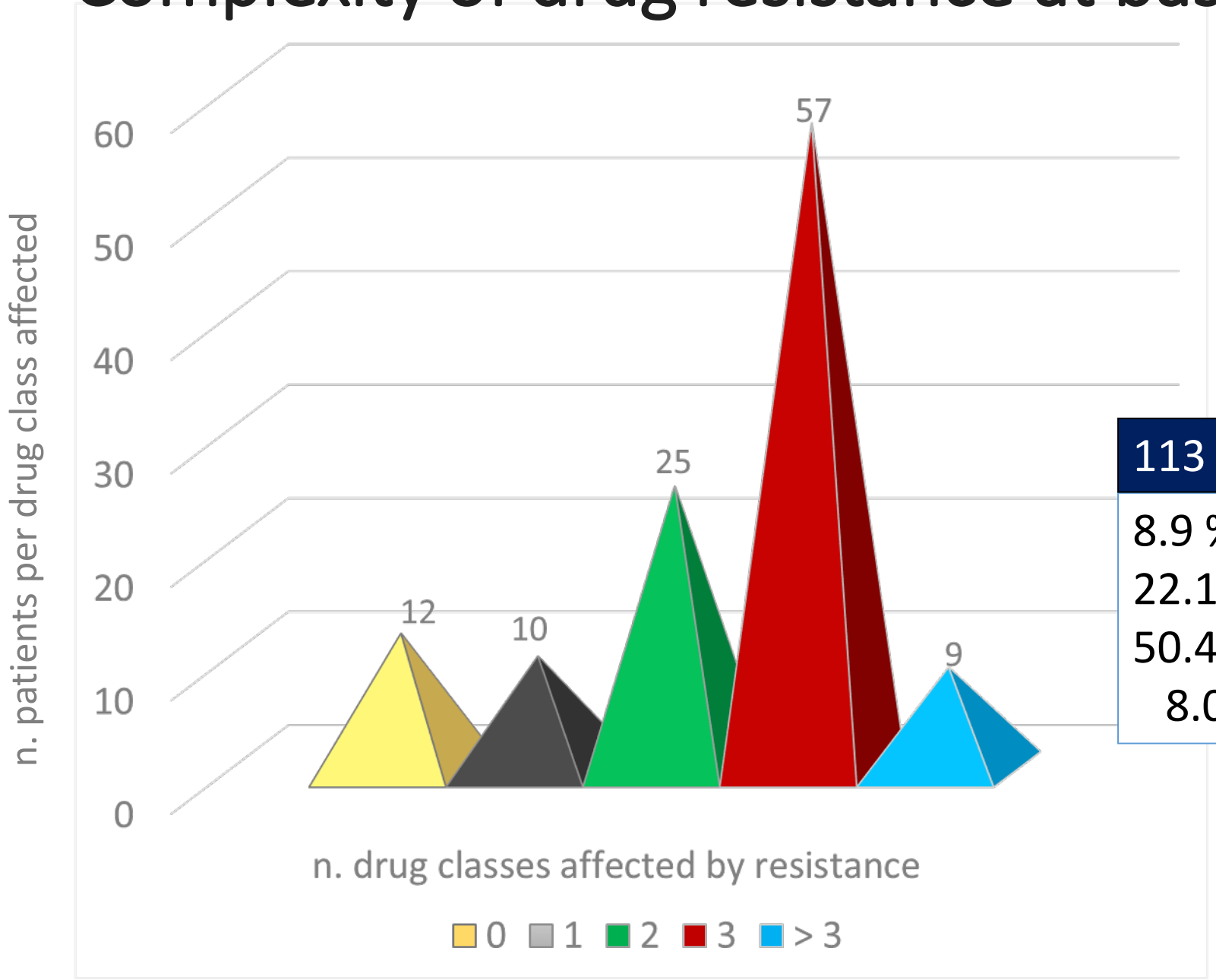


Frequency of single antivirals in the former regimen



DTG = dolutegravir, ddI = didanosine, ATV = atazanavir, /r = boosted with ritonavir, EFV = efavirenz, LPV = lopinavir, RPV = rilpivirine, MVC = maraviroc, ETV = etravirine, ABC = abacavir, 3TC = lamivudine, FTC = emtricitabine, TDF = tenofovir, RAL = raltegravir, DRV = darunavir

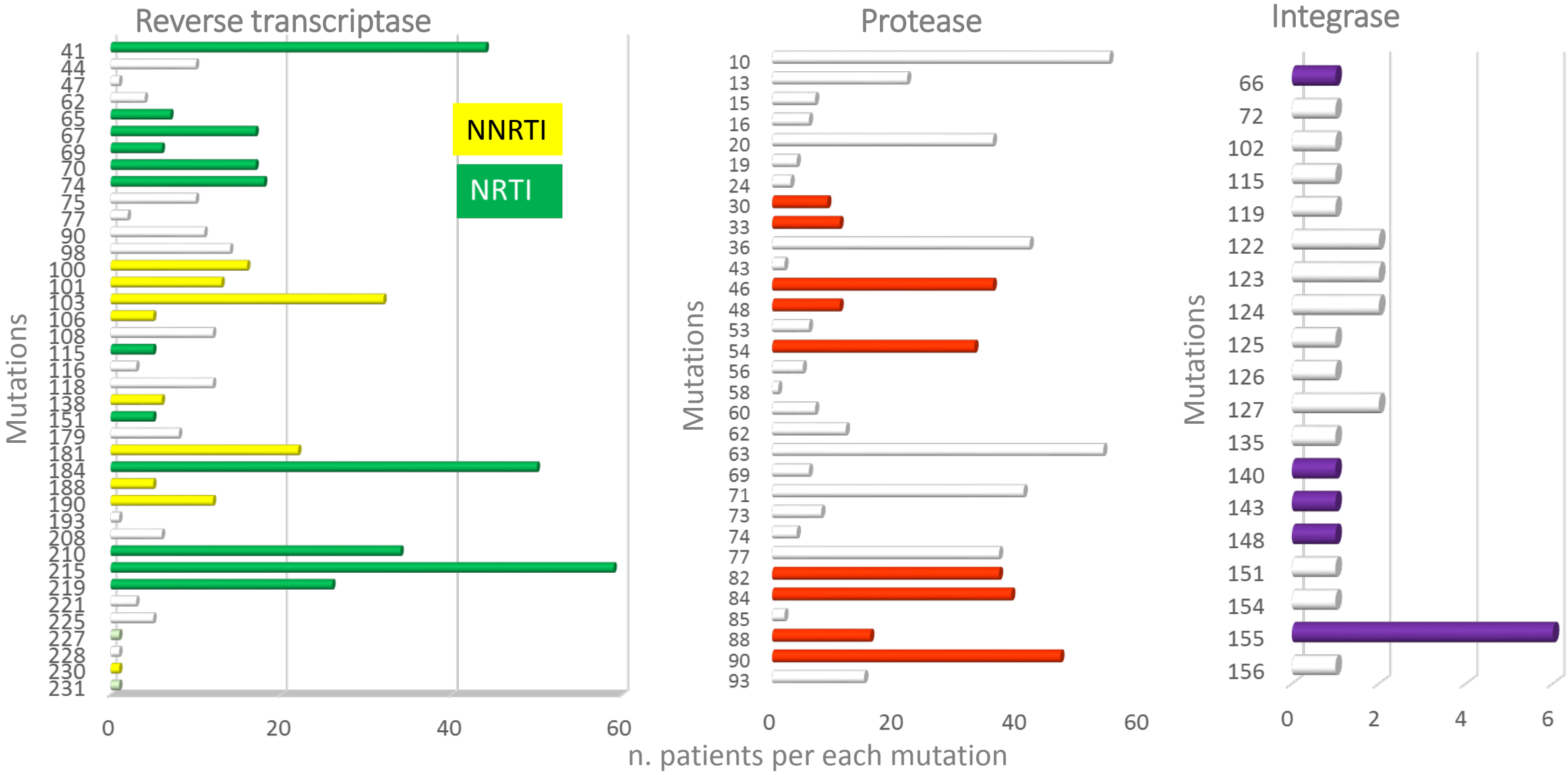
Complexity of drug resistance at baseline



113 subjects	
8.9 %	1 class
22.1%	2 classes
50.4%	3 classes
8.0 %	>3 classes

Frequency of single baseline mutations

83.2% NRTI mutations
80.5% PI mutations
10.6% INSTI mutations



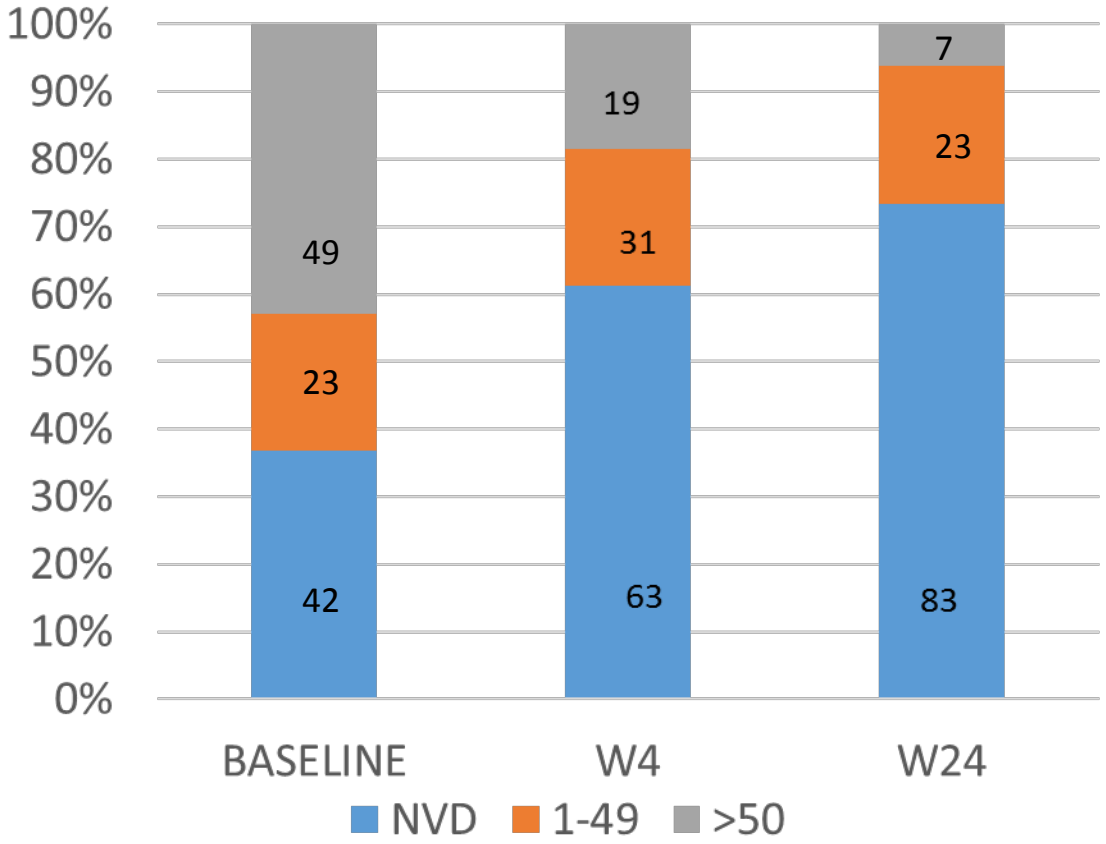
Results

One patient dropped out at week 24 for grade 2 elevation of liver enzimes

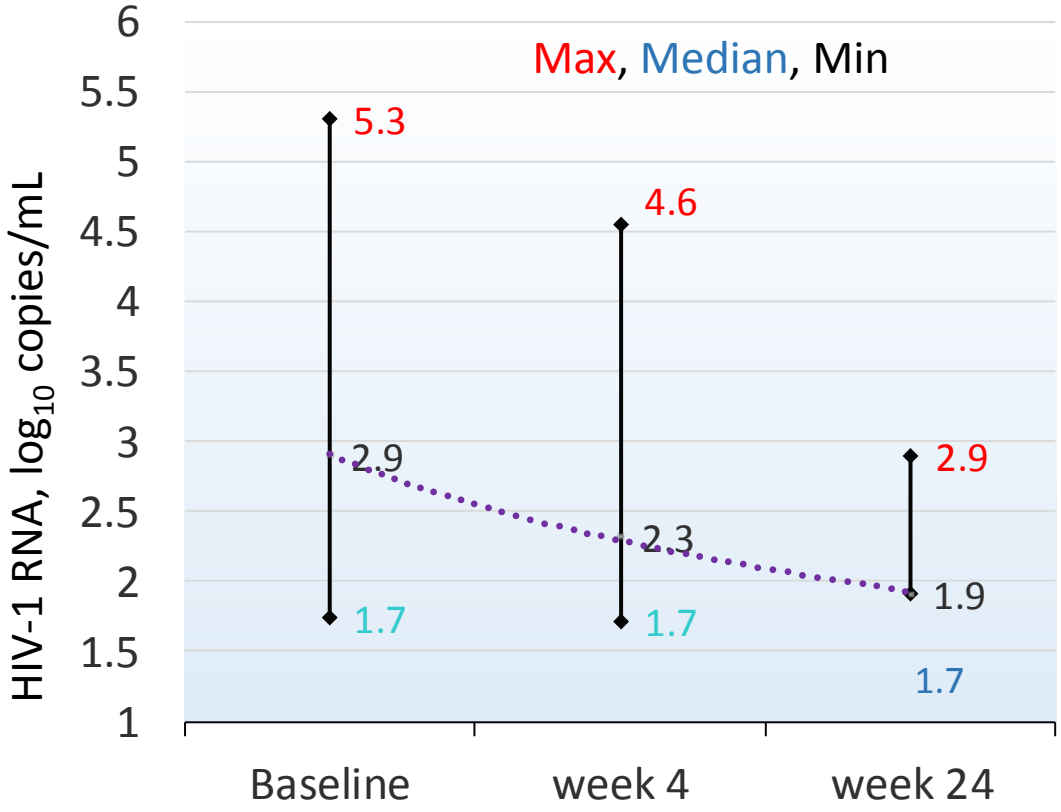
Beyond 24 week: 1 was lost to follow-up, 1 died of illicit drug abuse, 1 died of cancer-related sepsis.

Trend of HIV-RNA over follow-up, 24 weeks

Overall study population (n = 113) by HIV-1 RNA, copies/ml



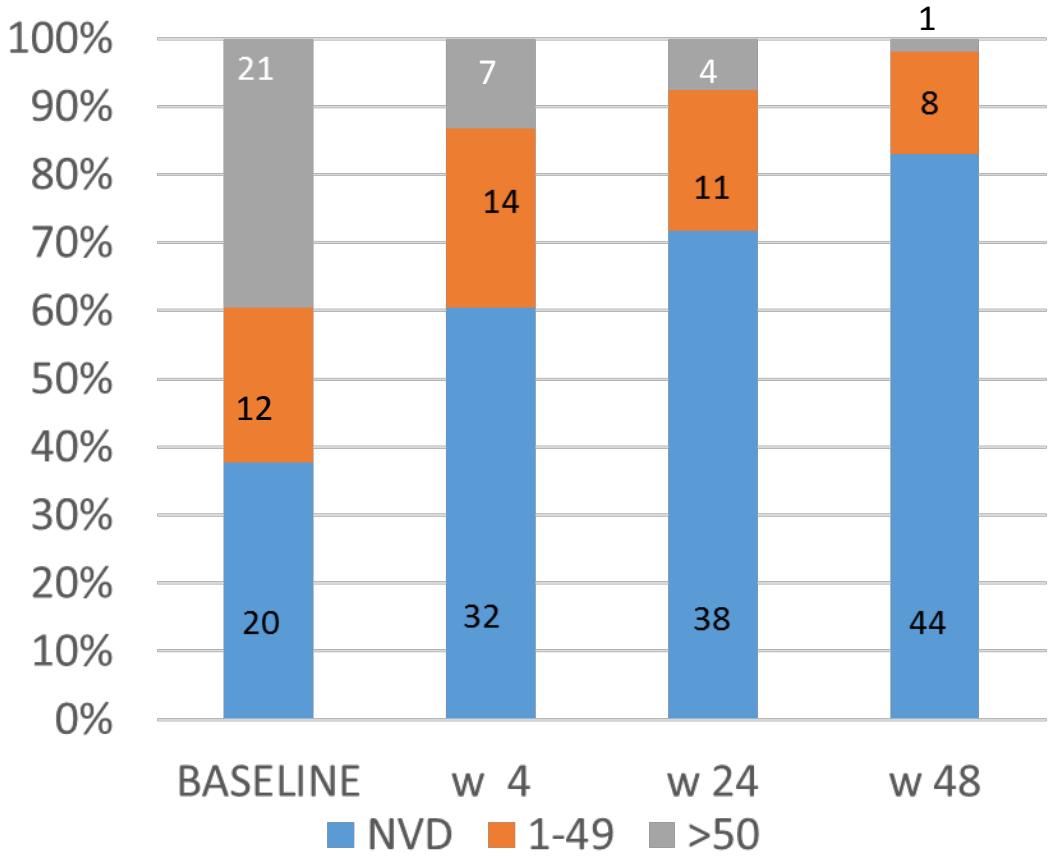
HIV-1 RNA decay in the subpopulation with baseline viral load >50 copies/mL (n= 49)



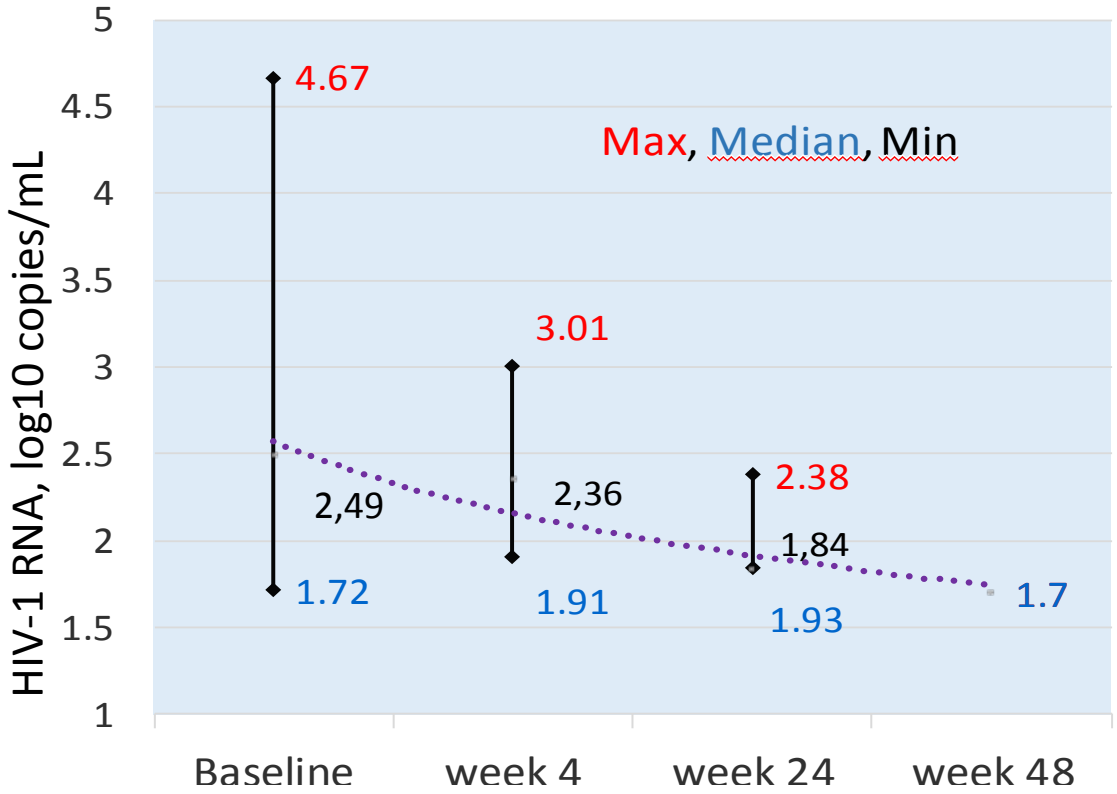
By week 24:
subject with HIV-RNA >50 copie/mL declined from 43.4% at baseline to 6.2%.
subjects in whom no virus was detected (NVD) increased from 37.2% at baseline to 73.5%.

Trend of HIV-RNA over follow-up, 48 weeks

48 week follow-up population (n = 53) by HIV-1 RNA (copies/mL)



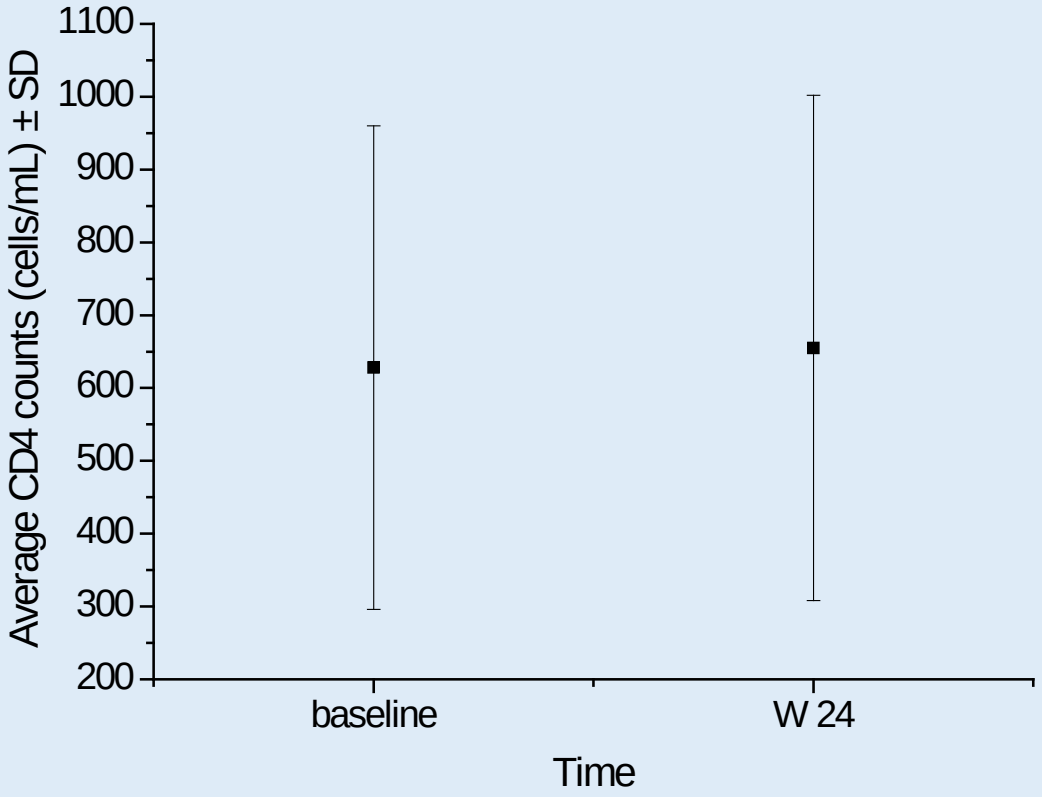
HIV-1 RNA decay in the subpopulation with baseline viral load >50 copies/mL (n=21).



By week 48:
subject with HIV-RNA >50 copie/mL declined from 39.6 % at baseline to 1.9 %
subjects in whom no virus was detected (NVD) increased from 37.7% at baseline to 83.0 % .

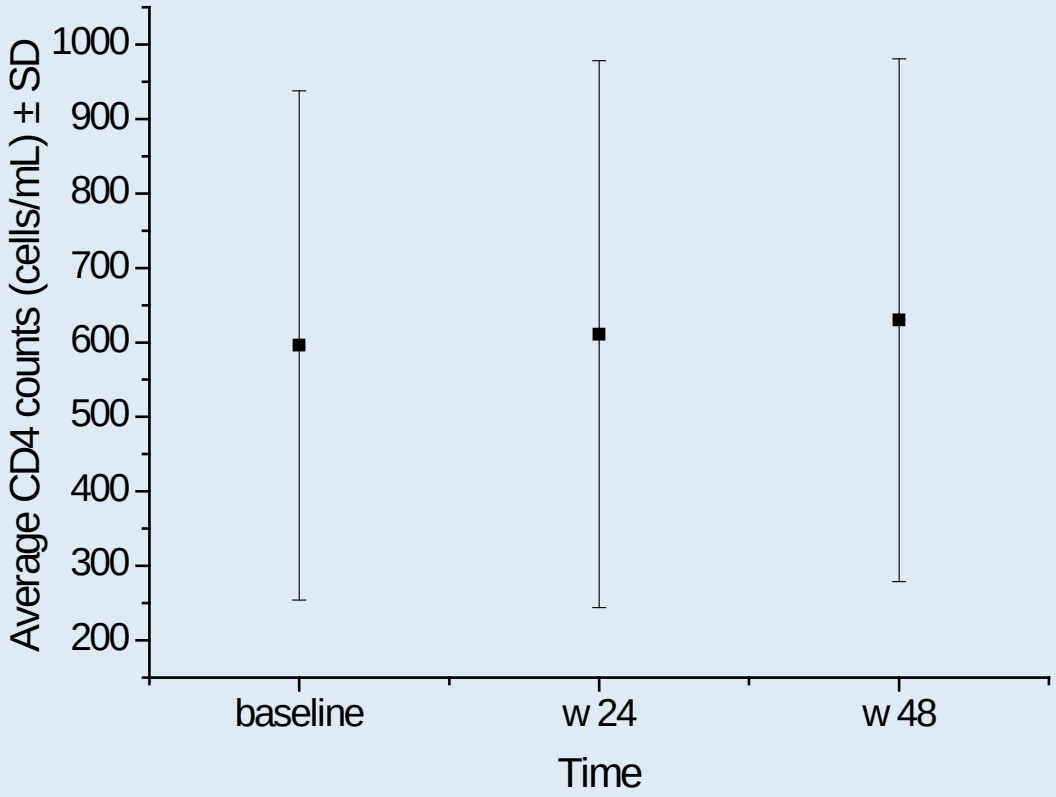
Trend of CD4 count over follow-up

Overall study population (n = 113), 24 week follow-up



Δ w24: mean + 8,9 DS ± 179,6

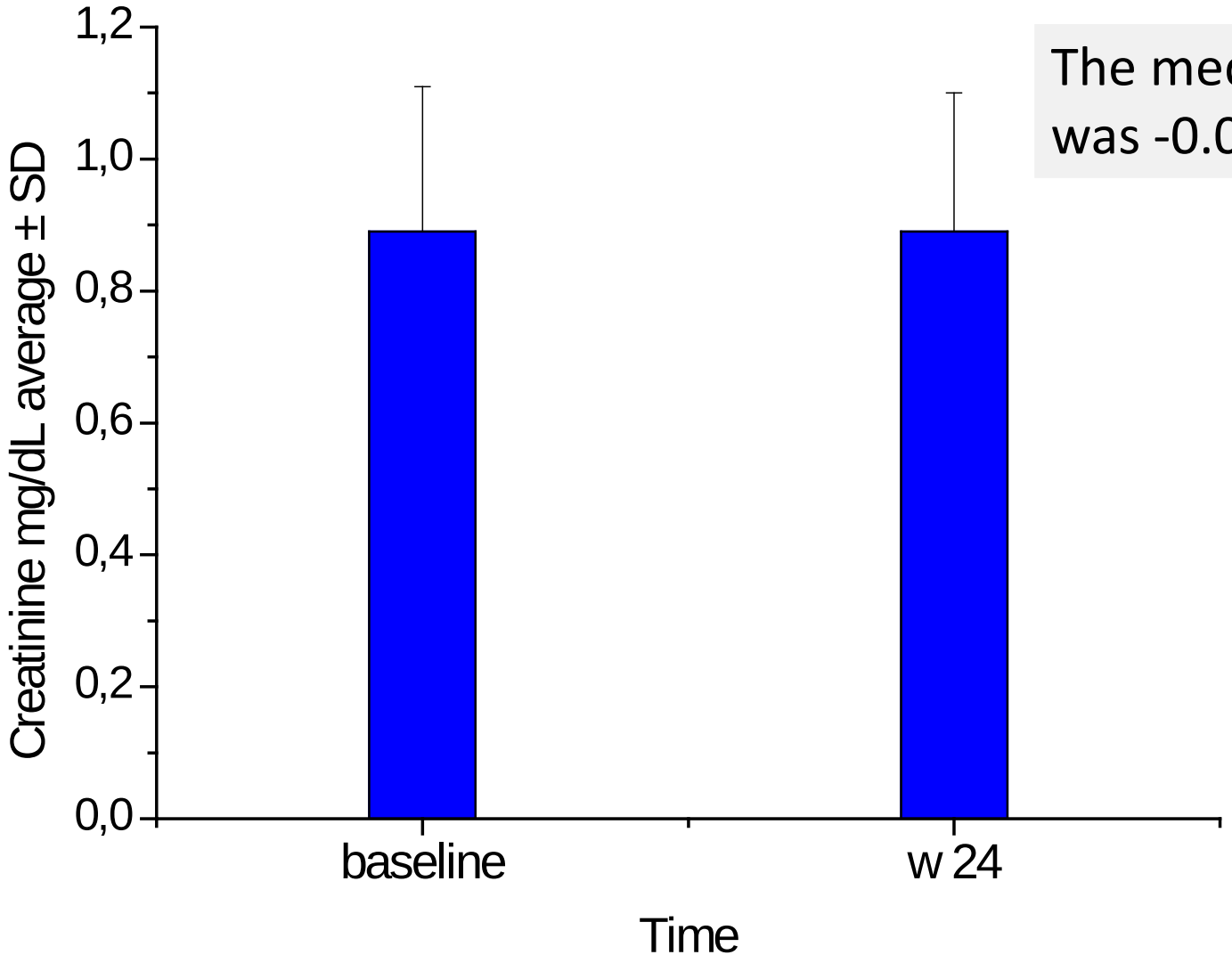
Subpopulation (n= 53), 48 week follow-up



Δ w48: mean +31,6 DS ±147,7

Δ= difference from baseline

Trend of creatinine over follow-up



The median variation in serum creatinine was -0.01 (range + 0.2 to – 0.21)

Conclusions

A dual regimen of DTG plus DRV/r proved:

✓Safe, with only one drop-out for toxicity

✓Effective, 93.8% of subjects <50 copies/mL at 24 w, 98.1% < 50 copies/mL a 48 w.

Eighteen subjects had reduced baseline sensitivity to darunavir (Stanford median score 15, range 15 – 40), but none failed. Eleven of these had a 24-week follow-up and 7 a 48-week follow-up.
Also, none of the subjects who had baseline INSTI resistance mutations failed.
No one developed new drug resistance mutations during the study.

✓CD4+ cell counts increase both in absolute values and in percentage, although not statistically significant.

✓In this cohort of highly drug-experienced patients, partly composed of subjects in overt failure of a salvage regimen and partly of simplifications of complex salvage regimens, the combination DTG plus DRV/r can provide the regimen safer and easier ever seen.

Aknowledgment to the Tivista (Tivicay plus Prezista Observational Cohort) Group

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