

Switch to Dolutegravir plus Rilpivirine dual therapy in cART-Experienced Subjects: an Italian cohort

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Background

- Little information is available about the efficacy and safety of the combination of rilpivirine (RPV) plus dolutegravir (DTG).
- The purpose of this work is to show the results of this regimen in clinical practice.

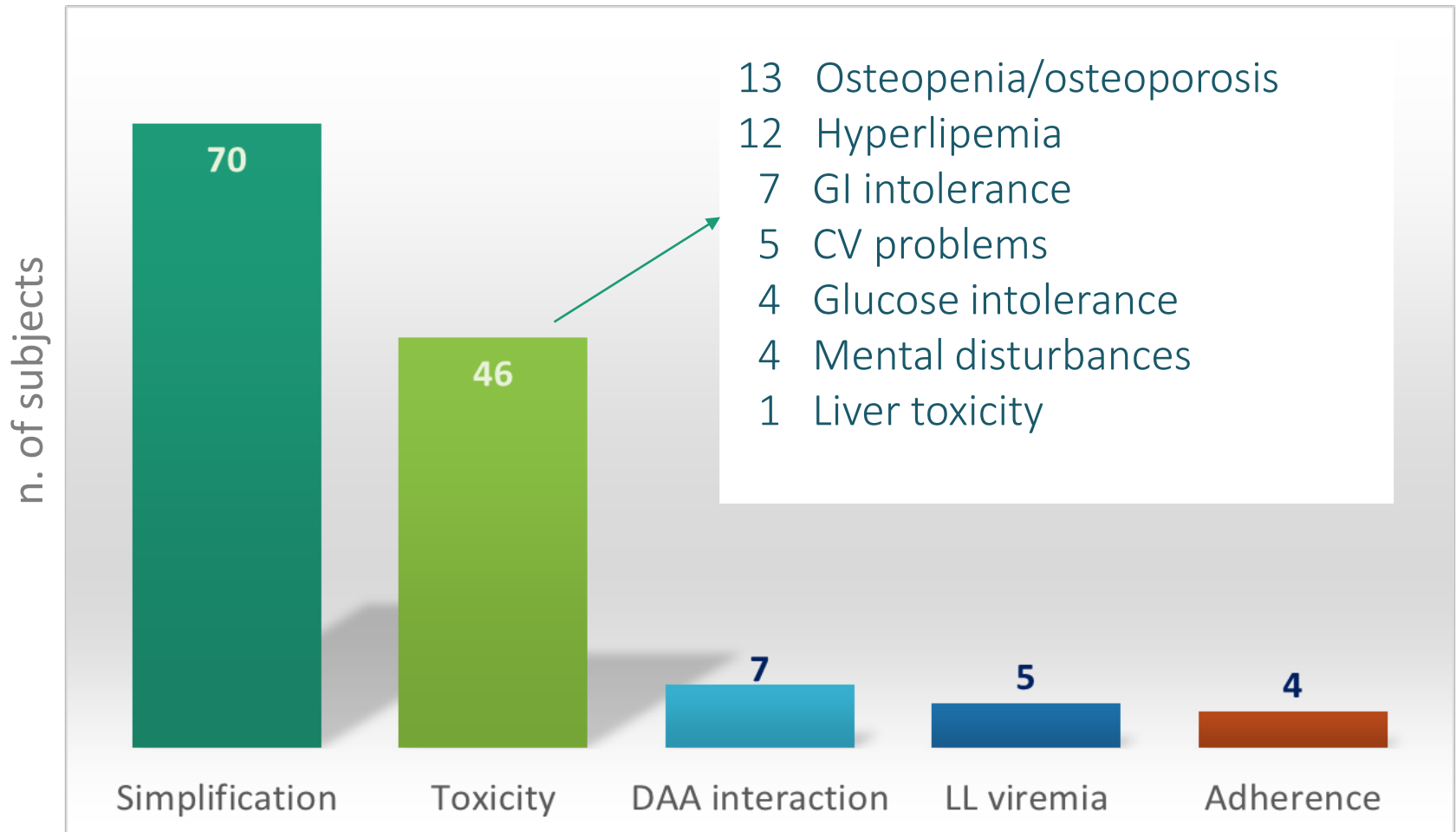
Methods

- All experienced HIV-1 infected subjects treated with DTG plus RPV in eight Italian centers were included between October 2014 and September 2015 in an observational cohort named TivEdO (Tivicay plus Edurant Observational Cohort).
- CD4+ cell counts, HIV-RNA and creatinine values were collected at baseline and 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 RNA, and virus not detected (NVD).

Baseline patient demographics, 132 subjects

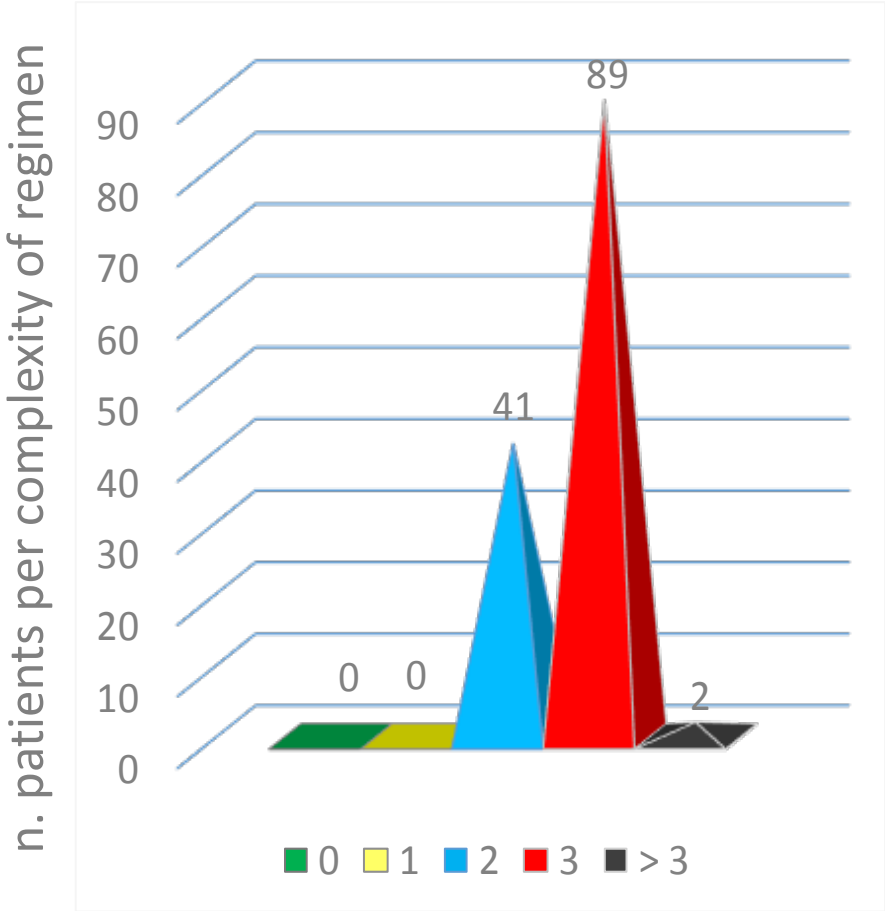
	Number (%)	Median (range)
Females/males	42/90 (31.7-68.3)	
Age, years		53 (29-77)
Non-caucasians	10 (7.6)	
Baseline CD4+ cell count (cells/ μ L)		708 (69-2615)
HIV-RNA, copies/mL		
•NVD	89 (54.9)	
•<50 quantifiable	27 (20.5)	
•>50	16 (12.1)	
Risk of transmission:		
Sexual transmission	91 (68.9)	
IDU	39 (29.5)	
Other	2 (1.5)	
At least 1 failure in previous regimens	57 (43.2)	
Follow-up (weeks)		29 (24-71)

REASONS TO SWITCH

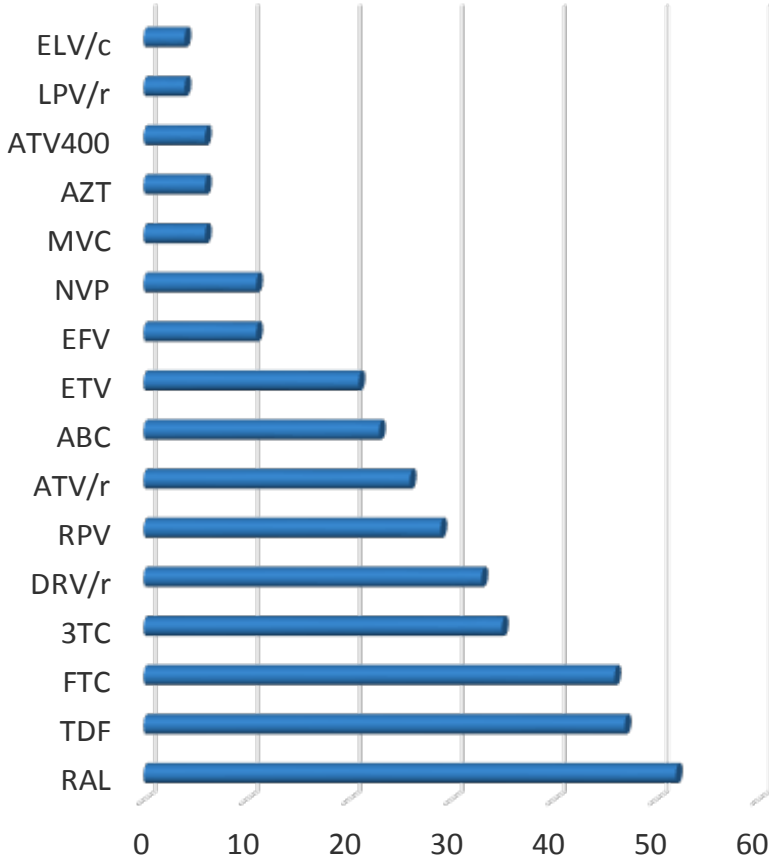


Patients' baseline disposition towards antiretrovirals

Complexity of the former regimen



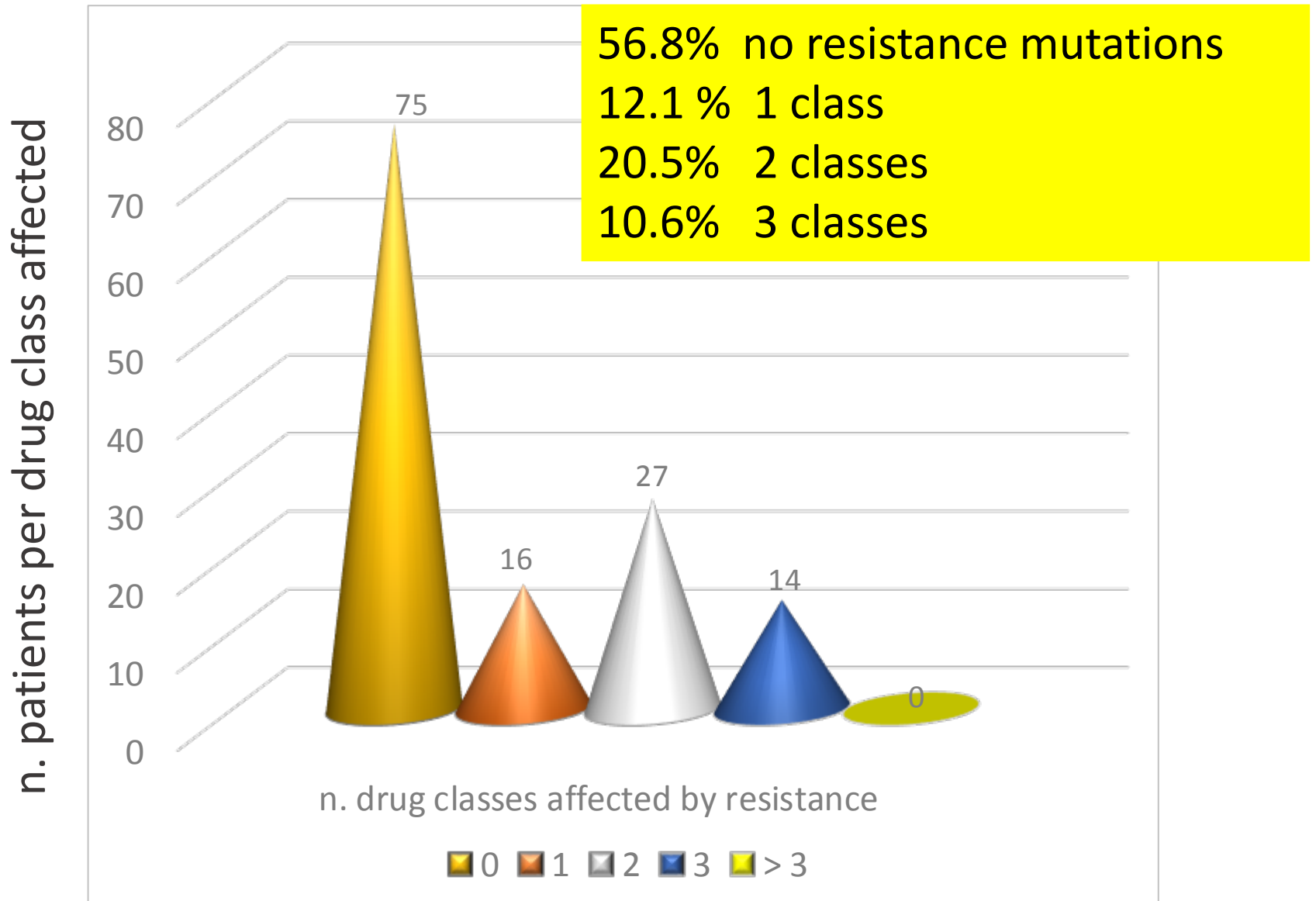
Antiretrovirals in the former regimen



n. drugs in previous regimen

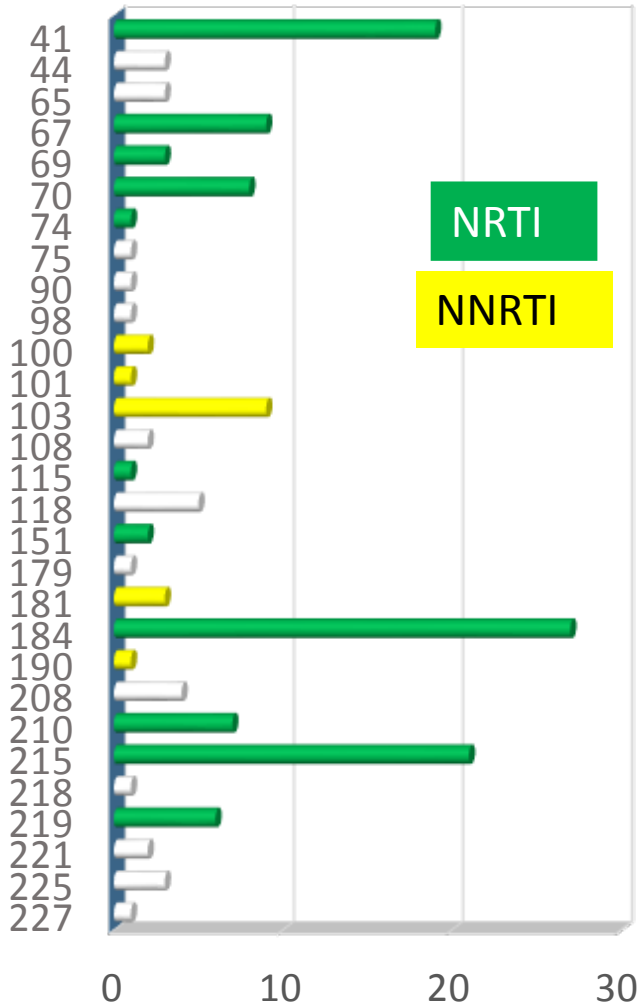
n. of patients

Complexity of drug resistance at baseline

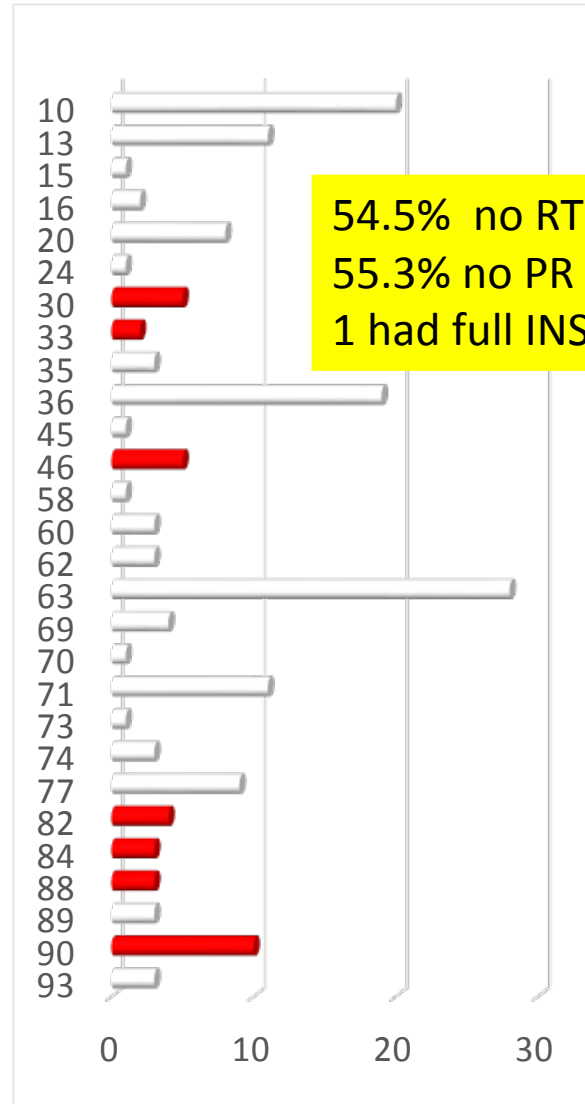


Frequency of single baseline mutations

Reverse transcriptase

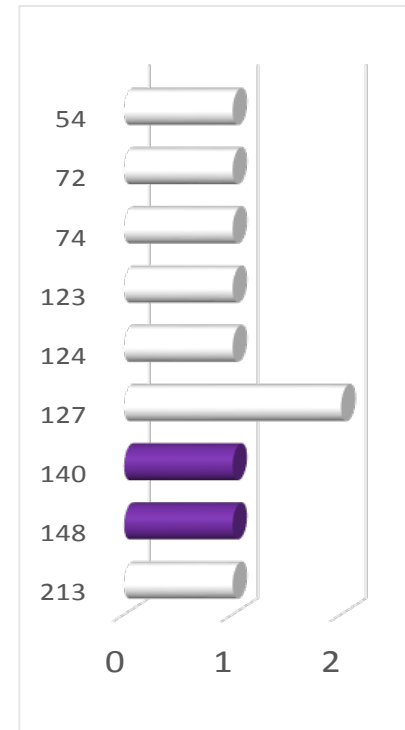


Protease



54.5% no RT mutations
 55.3% no PR mutations
 1 had full INSTI resistance

Integrase



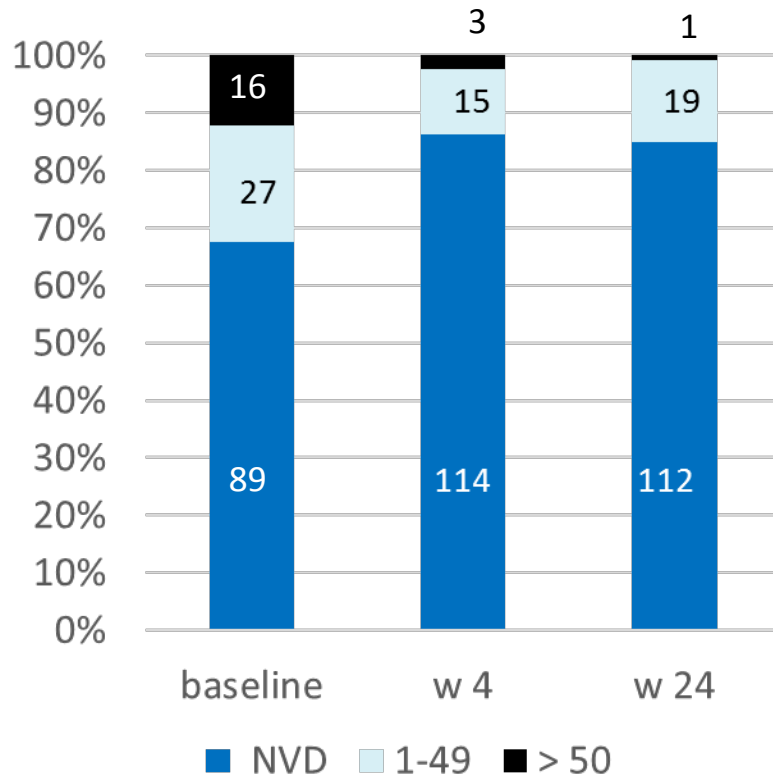
n. of patients per each mutations

Results

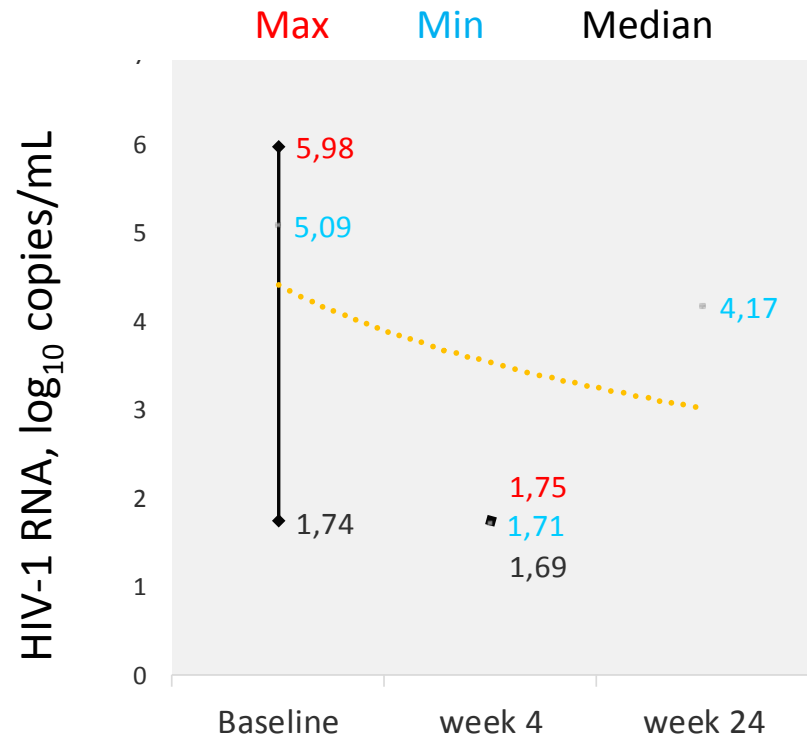
- One subject discontinued study drugs at week 24 for headache, one for drug interaction and one died after week 24 of illicit drug abuse.

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

Overall study population (n = 132) by HIV-1 RNA, copies/mL, at week 24



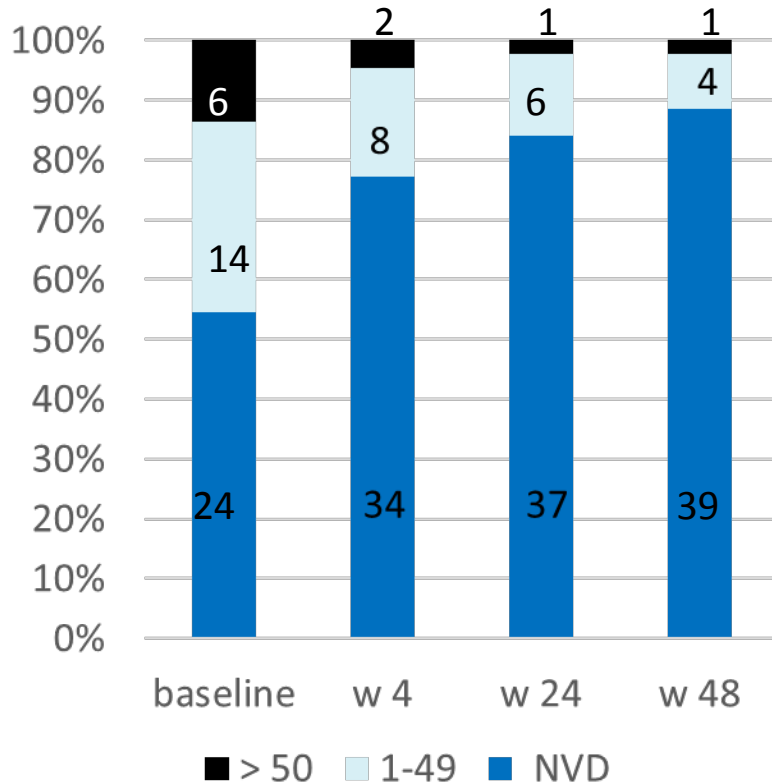
HIV-1 RNA decay in the subpopulation with measurable viral load, log₁₀ copies/mL (n=16)



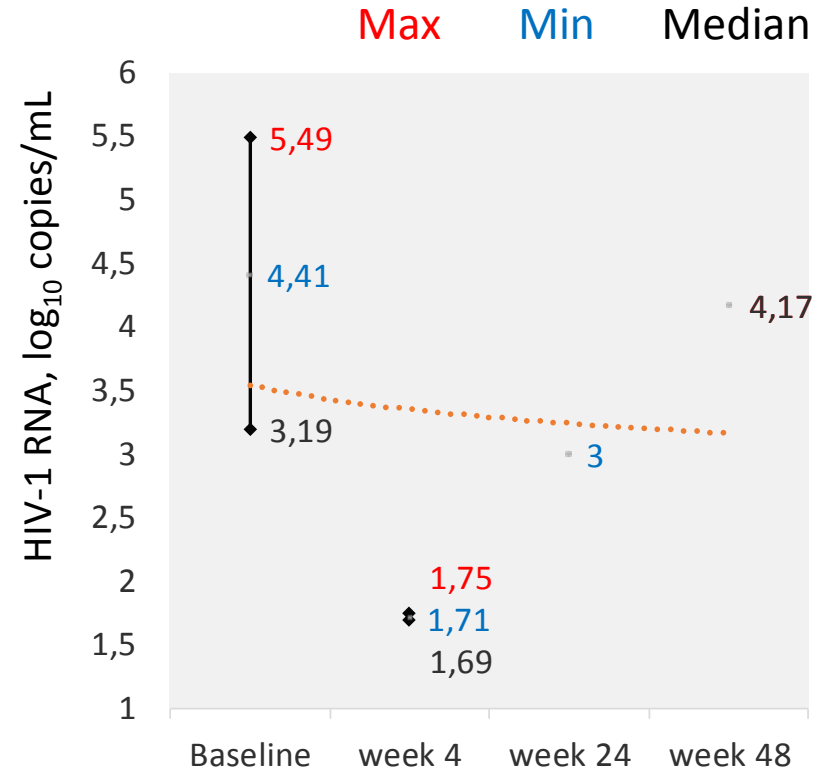
By week 24: subjects with HIV-RNA > 50 copie/mL declined from 12.1% at baseline to 0.8%; subjects in whom no virus was detected (NVD) increased from 67.4% at baseline to 84.4%.

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

Longer follow-up population (n = 44)
by HIV-1 RNA, copies/mL, at week 48



HIV-1 RNA decay in the subpopulation with
HIV RNA >50 copies/mL log₁₀ (n = 6)



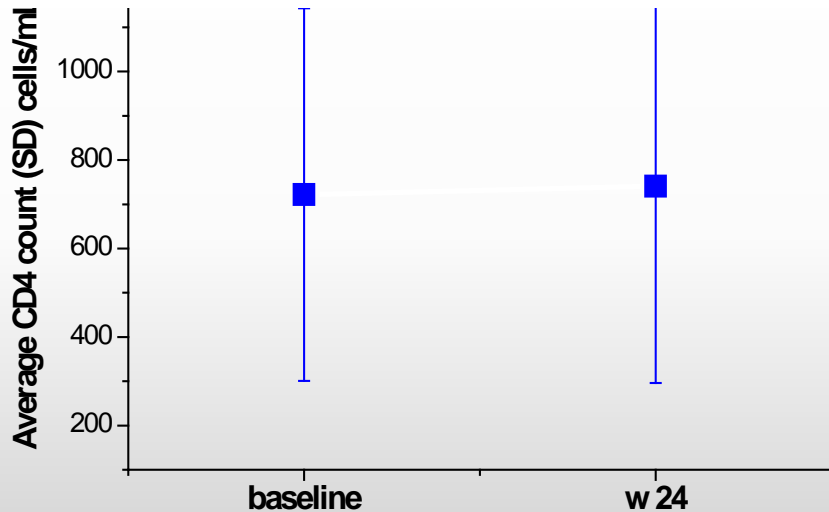
By week 48:

subjects with HIV-RNA > 50 copie/mL declined from 13.6 % at baseline to 2.3 %

subjects in whom no virus was detected (NVD) increased from 54.6% at baseline to 88.6 %

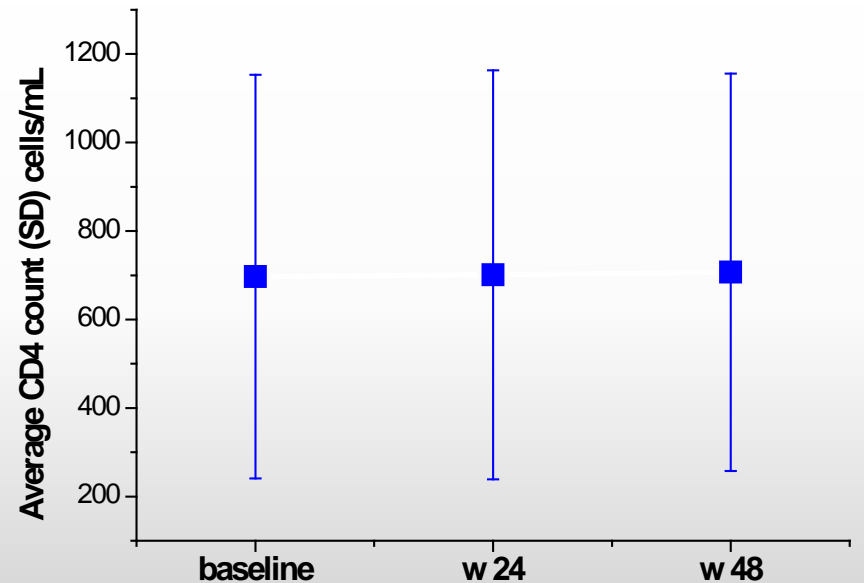
Trend of CD4 count over follow-up

Overall study population (n = 132), 24 w



Δ w24: mean + 8.89, range -499/+654

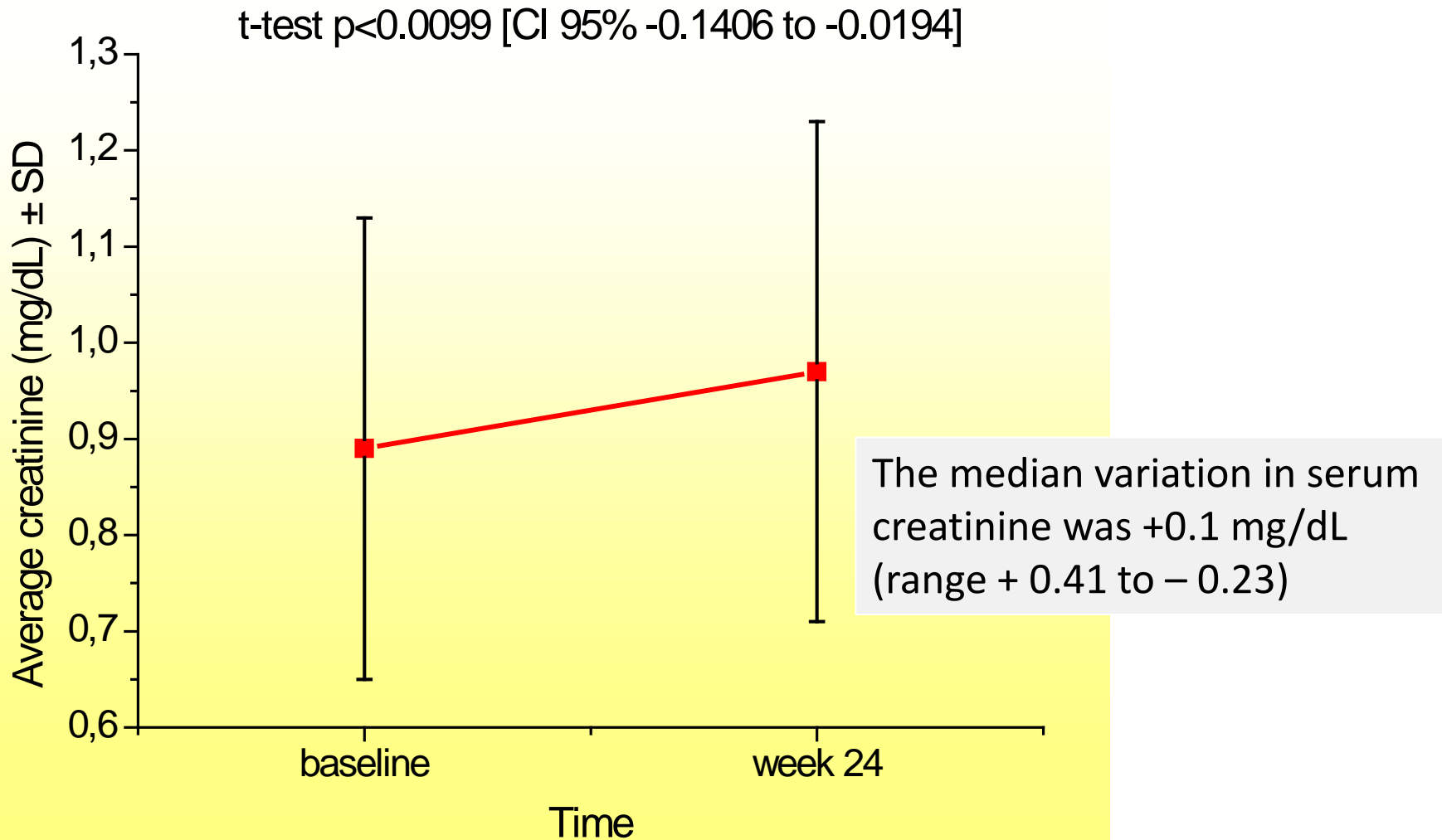
Subpopulation (n= 44), 48 w



Δ w48: mean +31.63, range -244/+263

Δ = difference from baseline

Trend of creatinine over follow-up



Conclusions

A dual regimen of DTG + RPV proved:

- ✓ Safe with only one drop-out for toxicity at week 24 for headache.
- ✓ Effective, 99.2% < 50 copies/mL both in the entire cohort at w 24 and in the week 48 subgroup. The proportion of subjects with any detectable viremia halved.

The subject with full INSTI resistance, is taking DTG twice daily having no other choice due to drug interaction and resistance.

One subject had baseline low-level resistance to rilpivirine, one intermediate and 4 high-level resistance (Stanford median score 50, range 15 – 70), but none failed, all having a 24-week follow-up.

One case of virologic failure, due to missed drug refill, with onset of new RT mutations 138Q and 181C, while the integrase gene was unaffected.

- ✓ CD4+ T-cells absolute count and proportion increased over time both in the entire cohort and in the week 48 subgroup although not statistically significant
- ✓ Serum creatinine increase was not clinically significant.
- ✓ Randomized clinical trials will definitely clear out the potential of this attractive regimen.

Aknowledgment to the Tivedo (Tivicay plus rilpivirine Observational Cohort) Group

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