ABSTRACT # 1

Virological and immunological response to treatment of naïve HIV-1 positive patients with viral load >500,000 copies/ml: do we need personalized treatment for this class of patients?

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Background

- Very little information is available about response to treatment of naïve patients with viral loads >500,000 copies/mL.

- *Mellors JV et al. Ann Intern Med* 1997. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection
  Plasma viral load is a single best predictor of progression to AIDS and death.

- Santoro MM et al. Antivir Ther 2013. Impact of pre-terapy viral load on virological response to modern first-line HAART
  Only 50 and 83% of patients with very high viral load >500Kcopies/mL reached undetectability at 24 and 48 weeks of therapy, respectively.

Aim of the study

- Main aim of the study was to understand whether a four drug regimen that includes raltegravir (RAL) works better in this population than a triple-drug regimen to reach a HIV viral load below the limit of detection (BLD) and may result in a better immune recovery.

Methods

- 194 naïve patients with VL >500,000 copies/mL, 93 AIDS presenters, no acute infection
- Three-drug regimen or four-drug regimen including RAL started January 2008 to December 2013
- Observation censored at 12 months
- Endpoint: % of patients with undetectable VL
- Virological failure defined as two consecutive VL > 50 copies/mL
- Statistical analysis was conducted with intention to treat methods.
  - Models were adjusted for regimen, nadir and baseline $CD4^+$ cell counts, age, AIDS at baseline. The time to reach undetectable VL was calculated using Kaplan Meier survival test. $CD4^+$ cell counts were evaluated at 3, 6, 9 and 12 months.

Patient baseline demographics, disease characteristics and antiretroviral regimens (194 subjects)

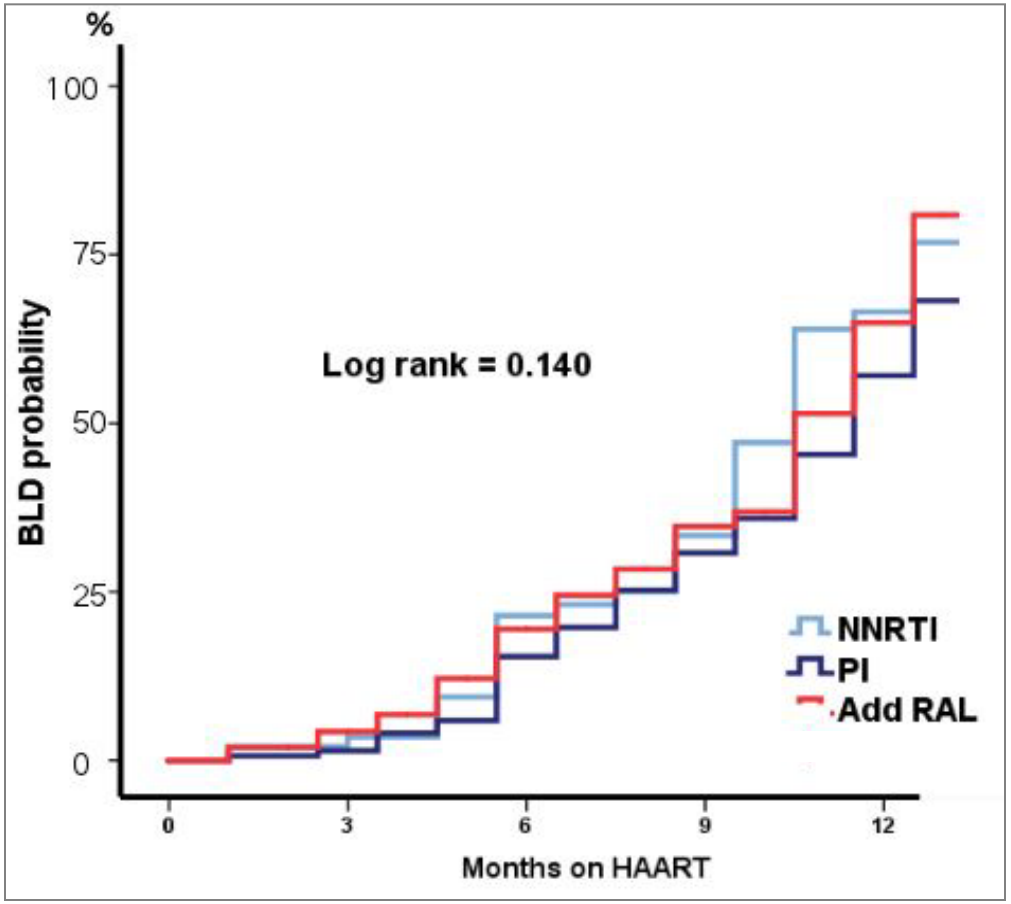
	Number (%)	Median (IQR)
Males	137 (70.6)	
Age, years		42 (35 - 51)
$CD4^+$ cells count (cell/µL)		100 (39 - 279)
HIV-RNA, Log_{10} (copies/mL)		6.0 (5.8 - 6.3)
$CD4^+$ cells count (cell/µL)(nadir)		88 (30 - 240)
Sexual transmission	166 (85.6)	
CD3 C3	93 (47.9)	
Class of antiretrovirals:		
PI/r-based regimens	159 (82)	
NNRTI-based regimens	35 (18)	
PI/r-based regimens + Raltegravir	33 (17)	
Duration of therapy with Raltegravir (months)		11.5 (4 - 12)

Probability of HIV viral load below the limit of detection

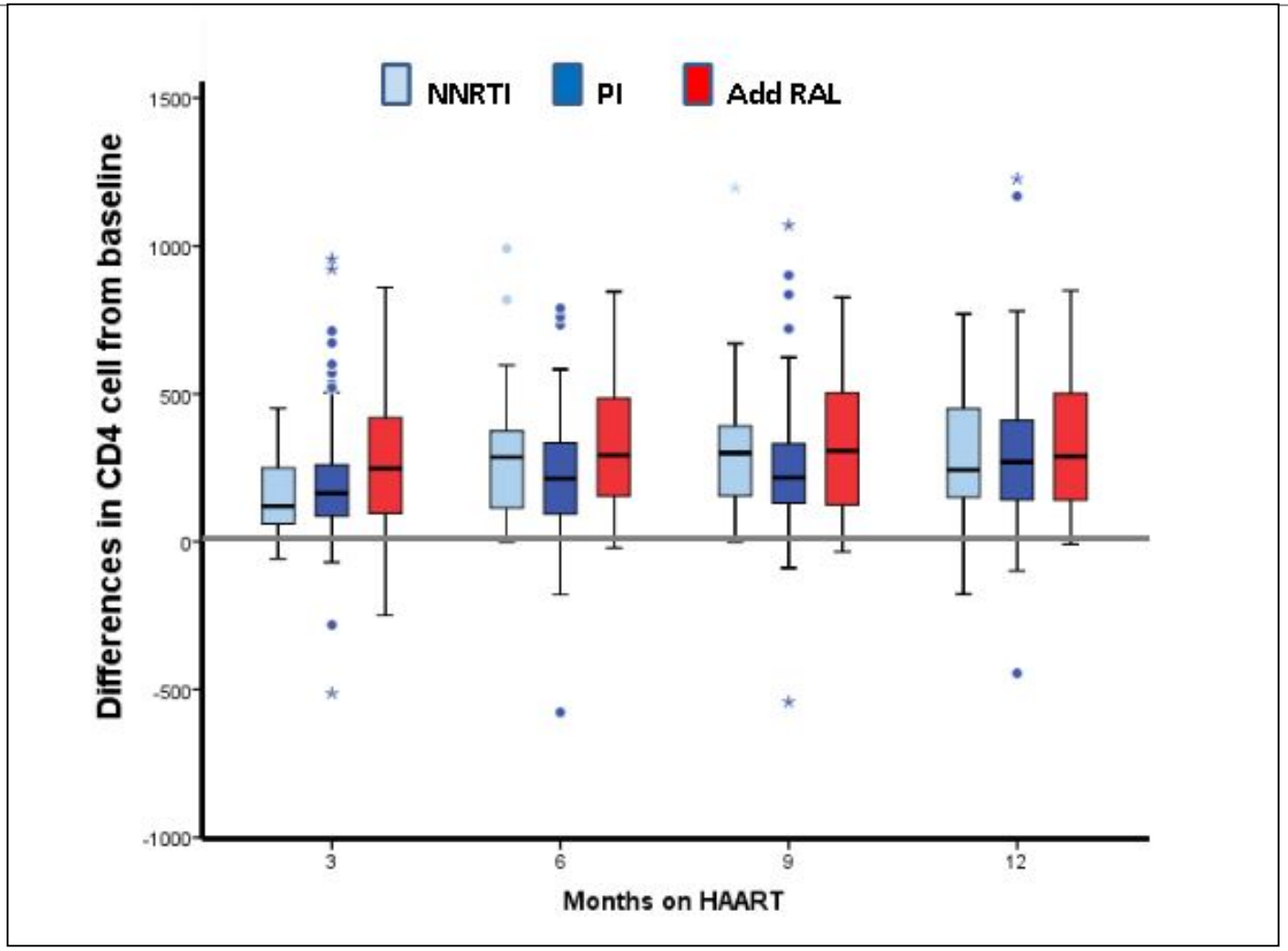
•Mean time to reach a HIV-RNA BLD was similar in the three groups (10.7 months)

•An undetectable viral load is achieved after three months in a higher percentage of subjects that add RAL 19.2% vs 12% with NNRTI and 12.5% PI, but this advantage is subsequently lost.

•Overall only 68.3% of the patients reached a HIV RNA below 50 copies/mL in the observed period regardless of the treatment used.



CD4 difference from baseline



The recovery of CD4 was similar with all the regimens used.

Multivariate analysis (use of INI or not)

	OR	IC 95% Lower	IC 95% Upper	P value
Age (per year)	1.04	1.00	1.07	**<0.026**
Male gender	1.50	0.65	3.44	0.345
CD4 nadir	1.01	1.00	1.02	0.246
AIDS	1.23	0.48	3.14	0.667
VL baseline	5.62	1.75	20.60	**<0.004**
CD4 baseline	0.99	0.98	1.01	0.271

Results

- For antiretroviral naïve patients with the highest viral loads clinicians prefer to use regimens containing PIs/r. However, PIs give no advantage compared to NNRTIs either in terms of recovery of $CD4^+$ lymphocytes or with regard to achievement of undetectable viral load.
- The choice of a standard regimen vs a four-drug regimen containing RAL was driven by higher baseline viral load
- Only 68.3% of naïve patients who began antiretroviral therapy with HIV-RNA >500,000 copies/mL had virological success at 12 months regardless of the treatment used.
- The gain of CD4 has been similar with all the regimens used and adding RAL to a standard regimen with PI/r did not improve CD4 recovery.
- Nine patients died during follow-up (8 AIDS related deaths).

Conclusions

- Personalized regimens in treatment-naïve patients with high viral loads are needed to improve virologic response.

- The faster VL decay shown with RAL vs. other drug classes in head-to-head triple therapy trials is not confirmed when a four-drug regimen with RAL is compared to standard therapy in highly viremic patient populations including many AIDS presenters

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