



# Impact of a 48-week Lopinavir/r Monotherapy on HIV1-DNA in Blood Cells in the MONARK Trial

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## ABSTRACT

### Background

The effect of HAART regimen on HIV-1 infected blood cells is estimated to be slightly lower than one log decrease after one year on treatment. The impact of protease inhibitor monotherapy on the reservoirs of HIV-1 infected cells is unknown and remains a concern. Our objective was to investigate in the MONARK trial, the effect on the cellular HIV-DNA reservoir of a lopinavir/r (LPV/r) monotherapy compared to a triple therapy including LPV/r+AZT/3TC. As a reminder, by on-treatment analysis, 56/67 (84%) patients in the LPV/r monotherapy arm had a plasma viral load (PVL) <50 copies/mL at W48.

### Methods

MONARK trial randomized antiretroviral naïve subjects with plasma VL <100,000cp/mL and CD4+ T cell count >100 cells/mm<sup>3</sup> to receive either LPV/r monotherapy or LPV/r-based triple combination. HIV-DNA levels in blood cells were measured both at baseline and Week 48 in both arms. It was quantified in whole blood samples, using the real time PCR HIV-1 DNA assay of ANRS AC11; the cut-off value was at 6 copies/PCR.

### Results

Overall, HIV-1 DNA samples were available in 102 and 72 patients at baseline and Week 48, respectively. Both arms were balanced at baseline, with 4.26 and 4.21 log copies/million CD4+ T cells in the monotherapy and triple-drug groups, respectively. A similar median decrease was observed at Week 48 in both arms: -0.75 log copies/million CD4+ T cells in the LPV/r arm versus -0.77 in the triple arm (p=0.88). There was no correlation between early HIV-RNA decrease and HIV-DNA decrease in both groups.

### Conclusion

Our results show a very similar effect of 48 weeks LPV/r monotherapy, versus a LPV/r-based triple regimen, on the level of the HIV circulating reservoir expressed by HIV-DNA level in blood cells in naïve patients. These data suggest that, at the cellular level, this LPV/r monotherapy regimen is potent, in comparison to a standard-of-care HAART.

MONARK is a prospective randomized trial comparing the safety and efficacy of lopinavir/ritonavir monotherapy to a standard lopinavir/ritonavir plus zidovudine and lamivudine regimen as an initial treatment regimen in HIV-1 infected patients with HIV RNA <100,000 copies/mL. The primary endpoint was the proportion of patients with HIV-RNA below 400 cp/mL at week 24 and below 50 cp/mL at week 48. The on-treatment analysis indicates that 80% and 95% of patients reached the primary endpoint in the monotherapy and triple-drug group, respectively (p=0.02).

## OBJECTIVES

Objective of this substudy: to investigate, in the MONARK trial, the impact of a LPV/r monotherapy compared to a triple therapy including LPV/r +AZT/3TC on HIV-DNA in blood cells

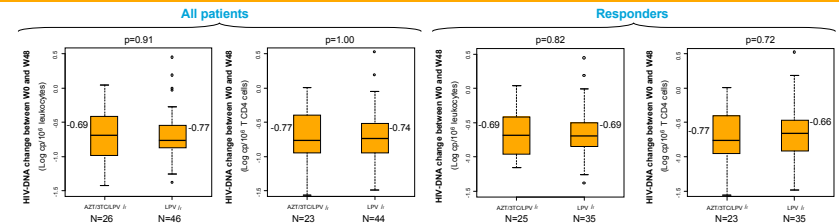
## PATIENTS AND METHODS

- A total of 138 patients were randomized in the trial, 83 in the LPV/r monotherapy arm, 53 in the triple therapy arm. HIV-DNA was quantified in 102 and 72 patients at baseline and week 48, respectively. In this substudy which considers patients entering in on treatment analysis, 52 patients were included in the group receiving a LPV/r monotherapy and 30 in the group receiving a triple therapy.
- HIV-DNA was quantified in whole blood using real-time PCR (amplification in the HIV-1 LTR gene – ANRS assay) at baseline and week 48, after extraction of total DNA and quantification by spectrophotometry. Results were expressed in copies/million leukocytes and copies/million T CD4 (using the blood formula). The cut-off value was 10 copies/PCR, i.e. 70 copies/million leukocytes.
- Patients included in the two groups of this substudy had similar immunological and virological characteristics at baseline: T CD4 cells count, HIV-RNA, HIV-DNA reported as cp/10<sup>6</sup> leukocytes and as cp/10<sup>6</sup> T CD4 cells.

	Group of patients receiving LPV/r				Group of patients receiving AZT + 3TC+ LPV/r			Statistics between two groups		Statistics between responders of two groups	
	All patients n=52	responders n=41	Non responders n=11	p (resp. vs non resp.)	All patients n=30	Responders n=29	Non responder n=1	p	p		
CD4 T cell count	234 [173; 294]	248 [195; 293]	182 [157; 295]	0.31	223 [166; 290]	226 [168; 290]	117	0.61	0.58		
Medians [IQR] at baseline											
HIV RNA log c/mL	4.4 [4.3; 4.7]	4.4 [4.3; 4.7]	4.8 [4.4; 4.9]	0.058	4.3 [4.1; 4.7]	4.3 [4.1; 4.7]	5.1	0.57	0.76		
HIV DNA log c/mL leukocytes	2.94 [2.7; 3.2]	2.93 [2.7; 3.2]	3.16 [2.9; 3.4]	0.075	2.91 [2.4; 3.1]	2.89 [2.5; 3.1]	3.6	0.39	0.54		
HIV DNA log c/mL CD4 T cells	4.3 [3.9; 4.5]	4.2 [3.9; 4.5]	4.5 [4.3; 4.7]	0.097	4.13 [3.7; 4.5]	4.07 [3.7; 4.5]	5.22	0.40	0.45		
<b>On-Treatment analysis</b>											
Proportion of patients with HIV-RNA	<400 c/mL at W24	50/52 (96%)			29/30 (97%)						
	<50 c/mL at W48	42/52 (81%)			29/30 (97%)						
Medians [IQR] at W48	CD4 T cell count	397 [319; 496]	409 [342; 538]	331 [288; 405]	0.11	378 [278; 543]	378 [278; 543]	0.94	0.62		
	HIV RNA log c/mL			2.47 [1.85; 2.52]				4.84			
	HIV DNA log c/mL leukocytes	2.18 [1.9; 2.5]	2.16 [1.9; 2.5]	2.19 [2.0; 2.6]	0.45	2.05 [1.9; 2.4]	2.05 [1.9; 2.4]	2.15	0.23	0.41	
	HIV DNA log c/mL CD4 T cells	3.49 [3.1; 3.7]	3.50 [3.1; 3.7]	3.49 [3.3; 3.6]	0.94	3.28 [3.1; 3.5]	3.28 [3.1; 3.5]	0.13	0.19		
	↑ CD4 T cells	+142 [105; 239]	+156 [106; 251]	+108 [65; 142]	0.13	+159 [108; 262]	+159 [108; 262]	0.53	0.82		
↓ HIV DNA log c/mL leukocytes	-0.77 [-0.5; -0.9]	-0.69 [-0.5; -0.9]	-0.80 [-0.7; -1]	0.078	-0.69 [-0.4; -1]	-0.69 [-0.4; -1]	-1.42	0.91	0.82		
↓ HIV DNA log c/mL CD4 T cells	-0.74 [-0.5; -0.9]	-0.66 [-0.4; -1]	-0.84 [-0.7; -0.9]	0.23	-0.77 [-0.4; -1.1]	-0.77 [-0.4; -1.1]		1.00	0.72		

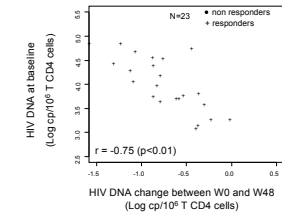
## RESULTS

HIV-DNA decrease after 48 weeks was not different between the 2 treatment arms and in responders of the two groups.

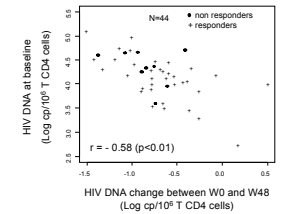


We observed a good correlation between HIV-DNA at baseline and HIV-DNA decrease during the first 48 weeks of treatment, in the 2 groups of patients.

Group of patients receiving AZT + 3TC + LPV/r



Group of patients receiving LPV/r



## CONCLUSIONS

- Our results show a similar HIV-DNA decrease after 48 weeks on a LPV/r monotherapy and on a standard LPV/r + AZT + 3TC triple therapy, in naïve patients. Lopinavir/r as a single drug agent appears potent to reduce the HIV circulating reservoir expressed by HIV-DNA level in blood cells, including in patients with high HIV-DNA at baseline.
- To our knowledge, this substudy is the first work demonstrating that HIV-DNA decrease during antiretroviral treatment is correlated with HIV-DNA at baseline, in both groups.

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