First line PI-containing regimens cause a greater decrease in bone mineral density compared NNRTI-containing regimens in HIV-1 infected patients: a substudy of HIPPOCAMPE–ANRS 121 trial.

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967

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BACKGROUND

No randomized study has evaluated the impact of different ARV regimens on the evolution of bone mineral density (BMD) at specific sites. We evaluated the change in BMD at hip and lumbar spine in patients initiating ARVs with one of the following regimens: PI/r/NNRTI (an NRTI-sparing regimen), PI/r/NRTIs or NNRTI/NRTIs.

PATIENTS AND METHODS

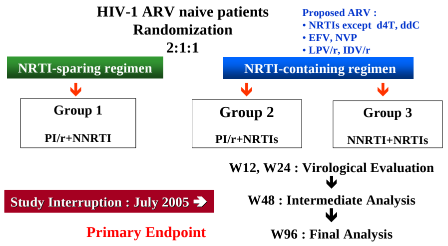
✓ Inclusion Criteria

- Age > 18 years
- ARV-naive
- Plasma HIV RNA (VL) > 5000 copies/ml
- CD4 cells ≤ 350/mm³ or CD4 cells > 350/mm³ plus VL ≥ 100 000 copies/ml
- Written informed consent

✓ Exclusion Criteria

- Acute opportunistic infection
- Pregnancy and/or breast feeding
- Systemic chemotherapy except for Kaposi's sarcoma
- Viral hepatitis B or C requiring a specific therapy
- Neutrophils < 750/mm³
- Hemoglobin < 8 g/dl, platelets < 20 000/mm³
- Creatinine < 1.5 X ULN; AST, ALT, bilirubin < 3 X ULN

✓ Statistical methods



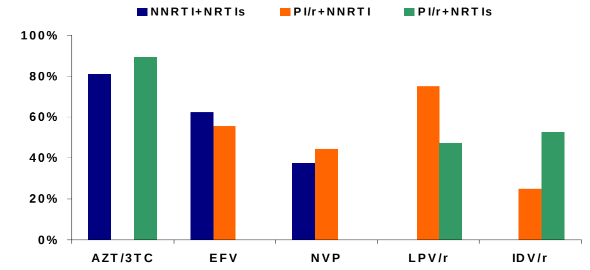
In a substudy, BMD at hip and at lumbar spine were evaluated at baseline and W48 by Dual Xray Absorptiometry (DEXA).

RESULTS

✓ Baseline Characteristics (N Total=71)

	NRTI-sparing regimen	NRTI-containing regimen		
	PI/r+NNRTI (n=36)	PI/r+NRTIs (n=19)	NNRTI+NRTIs (n=16)	**Total (n=71)**
Sex, n (%)				
Female	9 (25%)	3 (16%)	4 (25%)	16 (23%)
Male	27 (75%)	16 (84%)	12 (75%)	55 (77%)
Age, years, median (IQR)	40 (33 – 48)	41 (34 – 50)	37 (32 – 43)	40 (33 – 49)
Transmission group, n (%)				
Men who have sex with men	14 (39%)	13 (68%)	7 (44%)	34 (48%)
Heterosexual	19 (35%)	6 (32%)	8 (50%)	33 (46%)
Unknown//others	3 (8%)	0 (0%)	1 (6%)	4 (6%)
Origin, n (%)				
Caucasian	23 (64%)	15 (79%)	11 (69%)	49 (69%)
Black Africans	11 (31%)	3 (16%)	4 (25%)	18 (25%)
Others	2 (6%)	1 (5%)	1 (6%)	4 (6%)
Smokers, n (%)	21 (58%)	9 (47%)	11 (69%)	41 (58%)
BMI kg/M²	23 (20 – 25)	23 (21 – 24)	22(22 – 24)	23 (21 – 24)
Time since HIV-1 diagnosis (months)	6 (2 – 22)	7 (3 – 43)	13 (4 – 41)	6 (3 – 37)
CD4 count cells/mm³ (range)	226 (122 – 297)	251 (186 – 294)	207 (140 – 251)	219 (144 – 285)
Plasma HIV RNA log_{10} cp/ml	5.1 (4.5 – 5.5)	5.1 (4.3 – 5.5)	5.0 (4.5 – 5.5)	5.1 (4.4 – 5.5)

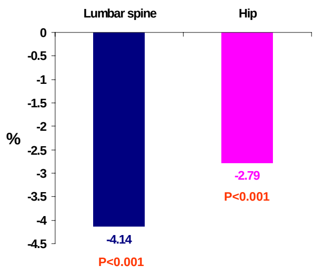
✓ Baseline treatment



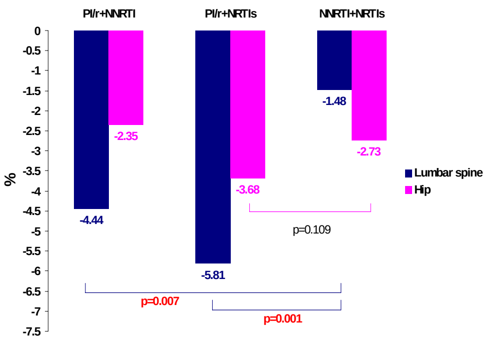
✓ Baseline T-Score

	NRTI-sparing regimen	NRTI-containing regimen		
	PI/r+NNRTI (n=36)	PI/r+NRTIs (n=19)	NNRTI+NRTIs (n=16)	**Total (n=71)**
T-score, median (IQR)				
Lumbar spine	-0.25 (-0.98 – 0.39)	-0.01 (-1.18 – 0.95)	-0.09 (-0.86 – 0.31)	-0.14 (-0.98 – 0.47)
Hip	0.12 (-1.14 – 0.69)	-0.01 (-0.32 – 1.05)	-0.20 (-0.76 – 1.46)	-0.01 (-0.88 – 0.83)
Osteopenia, n (%)	12 (33%)	6 (32%)	4 (25%)	22 (31%)
Lumbar spine	7 (19%)	6 (32%)	3 (19%)	16 (23%)
Hip	12 (33%)	1 (5%)	3 (19%)	16 (23%)
Osteoporosis, n (%)	2 (6%)	0 (0%)	0 (0%)	2 (3%%)
Lumbar spine	1 (3%)	0 (0%)	0 (0%)	1 (1%)
Hip	1 (3%)	0 (0%)	0 (0%)	1 (1%)

✓ The reduction in BMD between Baseline and W48



✓ The decrease in BMD at W48: Comparaison between groups



CONCLUSIONS

➢BMD was impaired in 31% of patients before starting any ARVs suggesting a causative role of HIV.

➢After one year of ARVs, there was a clinically significant decrease in BMD at hip and lumbar spine, comparable to what is observed in post-menopausal women.

➢After one year, the decrease in lumbar spine BMD was more pronounced in patients receiving either PI-containing regimen compared to NNRTI/NRTIs. BMD at specific sites should be monitored during lifelong ARV therapy.

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ANRS 121 study group