Limb and Trunk Fat Changes by Total Body DEXA After 96 Weeks of Treatment with Once-Daily (QD) Fosamprenavir (FPV) Boosted with either 100 mg or 200 mg of Ritonavir (/r) plus Abacavir (ABC)/Lamivudine(3TC): COL100758

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D.A. WOHL[1], E. DEJESUS[2], L. SLOAN[3], M. SENSION[4], Q. LIAO[5], K. PAPPA[5], K. OIE[5], C. HICKS[6]

[1]Univ of NC, Chapel Hill, NC, [2]Orlando Immun Ctr., Orlando, FL, [3] TX ID Consultants, Dallas, TX, [4]Comprehensive Care Ctr., Ft. Lauderdale, FL, [5]GSK, RTP, NC, [6]Duke Univ, Durham, NC

Abstract

Objectives: To evaluate changes in regional fat and bone mineral density (BMD) after 96 weeks of treatment with once-daily fosamprenavir boosted with two different doses of ritonavir (100mg vs. 200mg) in patients receiving ABC/3TC.

Methods: COL100758 was an open-label, randomized study evaluating FPV/r 1400mg/100mg (FPV/r100) or FPV/r 1400mg/200mg (FPV/r200) + ABC/3TC 600mg/300mg given once daily in 115 ART-naïve patients. Total body DEXA was obtained pre-treatment and at weeks 48, 72 and 96 using Hologic or Lunar scanners. Median percent changes in fat were reported for upper and lower limbs and trunk. Median percent change in total body BMD and L-spine BMD were reported (L-spine BMD data were only available from centers with Hologic scanners). P-values were obtained using Wilcoxon rank-sum test. Clinically relevant changes in fat mass were defined as >20% loss for limb fat and/or >20% gain in trunk fat.

Results: 71 patients had paired baseline and Week 96 DEXA scans (81% male, 58% non-white, median age 39 years). All results are reported as changes from baseline to 96 weeks for FPV/r100 (N=40) vs. FPV/r200 (N=31), respectively. The median percent change in fat mass in all regions studied was not significantly different between the study groups: -1.5% vs. +11.6% for upper limbs [p=.51], +10.0% vs. +16.3% for lower limbs [p=.39], and +14.5% vs. +18.5% for trunk [p=.88]. A >20% loss of fat was observed in upper limbs in 18% vs. 13% and in lower limbs in 15% vs. 6%; a >20% gain in trunk fat occurred in 38% vs. 45% of patients. No patient had simultaneous limb fat loss >20% and trunk fat gain >20%. Median total body BMD (g/cm2) percent changes were: -1.05% vs. -1.04 [p=.29], and -3.0% vs. -2.2% for the 27 patients with L-spine data [p=.68].

Conclusions: After 96 weeks treatment with once-daily FPV/r + ABC/3TC, both limb and trunk fat depots generally increased. Changes in regional fat were not significantly different between those assigned FPV/r100 vs. FPV/r200. BMD changes were small in both study arms.

Introduction

- Previously, we reported similar virologic and immunologic responses were achieved when FPV is boosted with 100 mg or 200 mg of ritonavir once daily in 115 ART-naïve patients also receiving ABC/3TC. [1]
- After 48 weeks of treatment, no significant differences were observed in the change from baseline in fasting cholesterol subsets or triglycerides. Additionally, there was no significant differences between study arms in change in limb fat or trunk fat; however, at 48 weeks there was a trend toward greater loss of bone mineral density (BMD) among those randomized to 200 mg of ritonavir. [2]
- We now present 96 week data on the differential affects of co-administration of FPV with 200 mg vs. 100 mg of ritonavir on body fat composition and BMD using whole body dual-energy X-ray absorptiometry (DEXA) in antiretroviral treatment-naïve men and women.

Methods

- **Study regimens**
  - Participants were randomized to receive 1400 mg of FPV once daily along with 100 mg of ritonavir (FPV/r100) versus 200 mg of ritonavir (FPV/r200). All received fixed dose abacavir/lamivudine (ABC/3TC), and (7) patients presumed hypersensitive to ABC were allowed to remain on study upon switching to zidovudine (ZDV)/3TC.
- **Body Fat Composition**
  - Whole body DEXA scans (using Hologic and Lunar Scanners) were obtained at study entry and weeks 48 and 96. 80% of patients were evaluated with Hologic scanners.
  - Changes in regional fat including combined upper limbs, combined lower limbs and trunk were compared between study groups. The proportion of patients in each group with >20% (combined) arm fat decrease, >20% (combined) leg fat decrease or >20% trunk fat increase were compared.
- **Bone Density**
  - Bone mineral density (BMD) was evaluated at study entry and weeks 48 and 96 by whole body DEXA scanning. Changes in total body and L-spine BMD were compared between study groups.
- **Adherence**
  - Pill counts were obtained at each visit and adherence calculated as total number of pills missing/total number of pills prescribed.
- **Statistical Methods**
  - Percent changes in arm fat, leg fat, trunk fat, and total body and L-spine BMD between the 2 treatment arms were compared using Wilcoxon rank-sum test. Comparisons of proportion of patients with clinically relevant fat changes were made using Fisher exact test.

Results

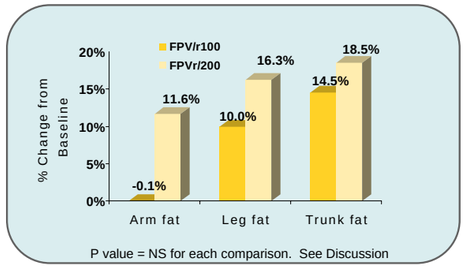
Table 1. Baseline characteristics of COL100758 population

	FPV/r100 (N=58)	FPV/r200 (N=57)
Median (range) age, years	39 (21-61)	40 (20-59)
Male	80%	81%
Race: Non-Caucasian	63%	55%
Caucasian	38%	46%
Ethnicity: Hispanic	20%	12%
Median (range) HIV-1 RNA, $\log_{10}$c/mL	4.70 (3.3, 5.9)	4.92 (3.3, 6.0)
HIV-1 RNA ≥100,000 c/mL (no, %)	20 (36%)	26 (46%)
Mean (SD) CD4 cell count, cells/mm^3	244 (148)	211 (173)
Mean (SD) Glomerular Filtration Rate (GFR) by MDRD in mL/min/1.73m^2	88.3 (18.9)	92.7 (16.2)
Median (range) total cholesterol/HDL-cholesterol ratio	4.59 (2.19, 32.0)	4.59 (1.95, 36.1)
Median (range) glucose (mg/dL)	91.8 (75.6, 149.4)	93.6 (77.4, 149.4)
Median (range) insulin (pmol/L)	65.0 (13.4, 519.6)	72.2 (13.4, 728.4)

Table 2. Baseline characteristics and 96-week change for 71 patients with paired DEXA scans

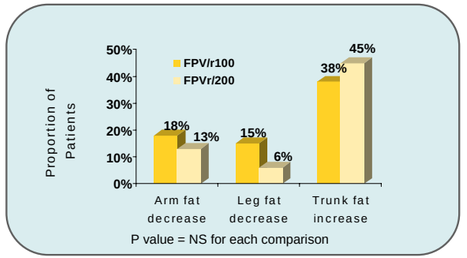
	FPV/r100 (N=40)			FPV/r200 (N=31)		
	Median	+/-Stand. Dev.,	(range)	Median	+/-Stand. Dev.,	(range)
Combined Arm Fat (g)						
Baseline value	1722	+/-2282,	(293-10751)	1490	+/-1172,	(255-4421)
Change from BL to Week 96	-18	+/-599,	(-2086-1024)	+76	+/-695,	(-1420-1832)
Combined Leg Fat (g)						
Baseline value	5659	+/-3697,	(1024-17519)	5815	+/-3343,	(1138-14583)
Change from BL to Week 96	+364	+/-2207,	(-3476-7766)	+1267	+/-1703,	(-2950-4875)
Trunk Fat (g)						
Baseline Value	9539	+/-6555,	(1311-31973)	7771	+/-5566,	(1199-20466)
Change from BL to Week 96	+1013	+/-2815,	(-2733-8766)	+1369	+/-2788,	(-3952, 10023)
Total BMD (g/cm^2)						
Baseline Value	1.22	+/-0.10,	(1.03-1.42)	1.20	+/-0.13,	(0.91-1.50)
Change from BL to Week 96	-0.01	+/-0.03,	(-0.07-0.05)	-0.01	+/-0.04,	(-0.10-0.04)
L-Spine BMD (g/cm^2)		(n=14)			(n=13)	
Baseline Value	1.20	+/-0.27,	(0.88-2.00)	1.12	+/-0.25,	(0.81-1.74)
Change from BL to Week 96	-0.04	+/-0.10,	(-0.25 - 0.10)	-0.02	+/- 0.10,	(-0.25-0.16)

Figure 1. Median percent changes in fat at Week 96



P value = NS for each comparison. See Discussion

Figure 2. Proportion of patients with >20% change from Baseline in regional fat at Week 96



P value = NS for each comparison

Table 3. Median percent adherence to study therapy by pill count of entire study cohort (n=115)

	FPV/r100	FPV/r200
% Adherence to Ritonavir	94.5%	88.8%
% Adherence to FPV	100%	100%
% Adherence to ABC/3TC	95.8%	92.1%

Figure 3. Median percent change in regional fat from Baseline through Week 96

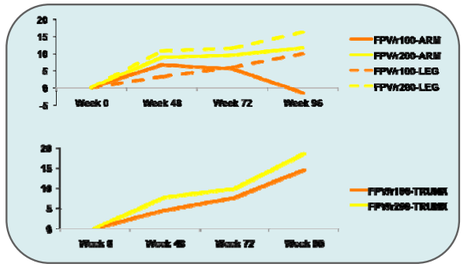
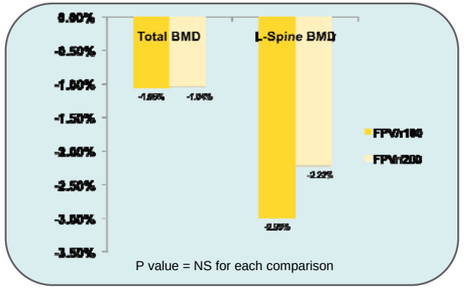


Figure 4. Median percent change in total and L-spine BMD at Week 96



P value = NS for each comparison

Discussion

- **After 96 weeks of therapy with FPV/r + ABC/3TC:**
  - **Leg and trunk fat increased in both the FPV/r100 and FPV/r200 study groups.**
  - **Arm fat increased early during study follow-up but had returned to baseline among those receiving FPV/r100. The difference between study groups in the change in arm fat at Week 96 was not statistically significant (p=0.52) and there was considerable variability in values within each group.**
  - **No patient with available paired Baseline and Week 96 DEXA data had simultaneous increases>20% in trunk fat and either combined arm or leg fat decreases >20%.**
  - **There were no statistically significant differences between study groups in the median changes in regional body fat.**
  - **L-spine BMD dropped by 2%-3% within the group of 27 subjects who had data available, with no significant difference observed when comparing the study arms.**

Conclusions

- **As has been observed in other recent trials among treatment-naïve patients, limb and trunk fat increased during the study, while BMD tended to decline.**
- **In addition to providing similar virologic and immunologic responses among 115 treatment-naïve study participants, dosing of FPV with 100 mg *versus* 200 mg of ritonavir daily was not associated with significantly different changes in regional fat depots, BMD or fasting lipid parameters (data not shown).**
- **The effect of differential adherence to ritonavir between the two arms on changes in metabolic parameters is worth examination. However, overall levels of adherence to ritonavir in this trial were high (>88%).**

Acknowledgements

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References

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