

NRTI Sparing Trial (CTN 177): Antiviral and Metabolic Effects of Nevirapine (NVP) + Lopinavir/ritonavir (LPV/r) vs. Zidovudine/lamivudine (AZT/3TC) + NVP vs. AZT/3TC + LPV/r

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OBJECTIVES

To compare changes in viral load, CD4 cell count, fasting lipids, glucose, and lactate in patients randomized to an NRTI-sparing regimen (NVP/LPV/r) or one of 2 NRTI-based regimens (AZT/3TC with either NVP or LPV/r)

METHODS

STUDY DESIGN

- Open-label, 96-week multicentre trial
- 78 antiretroviral-naïve adults were randomized 1:1:1 to receive one of:
 - NVP 200 mg bid* + LPV/r 533/133 mg bid
 - LPV/r 400/100 mg bid + AZT 300 mg bid + 3TC 150 mg bid (as Combivir)
 - NVP 200 mg bid* + AZT 300 mg bid + 3TC 150 mg bid (as Combivir)

*following 2-week 200 mg once daily lead-in dose

CLINICAL AND LAB ASSESSMENTS

- At weeks 0, 12, 24, and 48
- Plasma viral load (pVL)
- CD4 cell count
- Fasting lipids
 - Total cholesterol (TC)
 - HDL cholesterol
 - LDL cholesterol
 - Triglycerides
- Fasting glucose
- Lactate

STATISTICAL ANALYSIS

- Categorical variables were compared between groups using the Chi-square Test or Fisher's Exact Test, as appropriate.
- For continuous variables, medians and inter-quartile ranges were calculated and comparisons made using the Kruskal-Wallis Test, due to deviations from the Normal distribution in many cases.
- P values > 0.05 are considered not significant (NS).
- All pVL results >75,000 copies/mL were set to 75,000 (4.9 log₁₀) for the analysis, due to different upper limits of detection for pVL assays at various sites.
- The **metabolic analysis** includes 51 patients who have lipid data at baseline and weeks 24/48.
- The **efficacy analysis** includes all 77 eligible patients (1 randomized patient was ineligible).

Metabolic analysis (n=51)

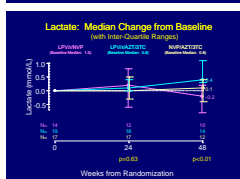
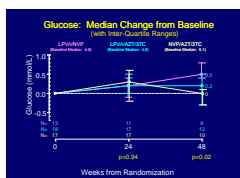
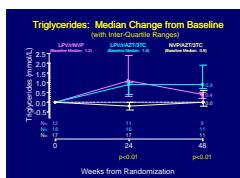
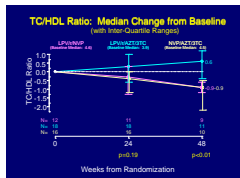
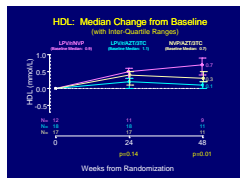
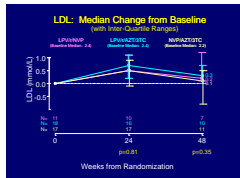
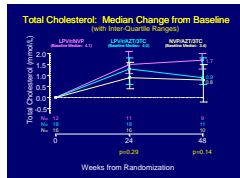
RESULTS

	LPV/r NVP	LPV/r AZT/3TC	NVP AZT/3TC
N	14	20	17
N (% Male)	12 (86)	17 (85)	11 (65)
Age (years)*	34.7	36.5	38.0
CD4 (cells/mm ³)†	217	240	210
CD4 fraction**	15.5%	17.3%	16.0%
pVL (log ₁₀ copies/mL)†	4.9**	4.9**	4.9**
Weighting ratio†	0.9	0.9	0.9
Body mass index*	21.6	23.4	22.0

No statistically significant differences were observed among treatment arms.
*Median. **The upper limit of detection (75,000 copies/mL).

	LPV/r NVP	LPV/r AZT/3TC	NVP AZT/3TC
Total cholesterol (mmol/L)	4.1	4.0	3.4
HDL cholesterol (mmol/L)	0.9	1.1	0.7
LDL cholesterol (mmol/L)	2.4	2.6	2.2
TCHDL ratio	4.6	3.9	4.5
Triglycerides (mmol/L)	1.2	1.0	0.8
Glucose (mmol/L)	4.8	4.8	5.1
Lactate (mmol/L)	1.5	0.8	0.8

No statistically significant differences were observed among treatment arms.



CONCLUSIONS

Among patients remaining on study at week 48:

- NVP may counteract the adverse impact of LPV/r on lipids: favourable changes in HDL cholesterol and total cholesterol/HDL ratio were seen in both NVP-containing arms
- Lactate increased in the arms containing AZT/3TC and decreased in the NRTI-sparing arm
- Analysis of mitochondrial DNA/nuclear DNA ratio is pending

Efficacy analysis (n=77)

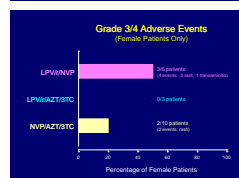
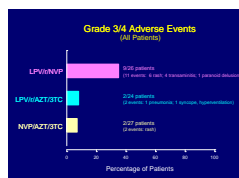
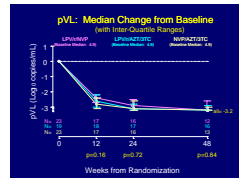
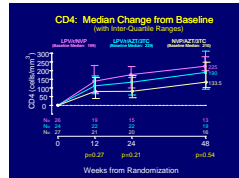
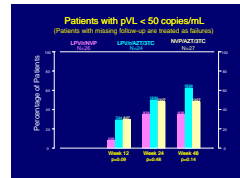
RESULTS

	LPV/r NVP	LPV/r AZT/3TC	NVP AZT/3TC
N	26	24	27
N (% Male)	20 (77)	21 (88)	17 (63)
Age (years)*	36.0	37.0	38.1
CD4 (cells/mm ³)†	199	229	210
CD4 fraction**	16%	16%	15.0%
pVL (log ₁₀ copies/mL)†	4.9**	4.9**	4.9**

No statistically significant differences were observed among treatment arms.
*Median. **The upper limit of detection (75,000 copies/mL).

Subject disposition

	Week 48		
	LPV/r NVP	LPV/r AZT/3TC	NVP AZT/3TC
On study	15	19	19
Off/late to adherence	7	2	5
Off/late to VL failure	0	0	1
Lost to follow-up	3	3	1
Did not start	1	0	1
Total randomized	26	24	27



CONCLUSIONS

At week 48:

- No differences were seen among arms with respect to pVL and CD4 outcomes (for patients remaining on study: on-treatment analysis)
- No statistically significant differences were seen in pVL outcomes by intent-to-treat analysis, but only 9/26 patients (35%) randomized to LPV/r/NVP have pVL<50 copies/mL at weeks 24 & 48
- This appears to be due to dropouts related to more rash and hepatic adverse events with LPV/r/NVP, especially in women

NRTI-sparing Study Investigators

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