Abstract # 962

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Switching from Lopinavir/Ritonavir (LPV/r) Soft Gel Capsule (SGC) to Tablet Formulation improves Tolerability in Indigent AIDS Clinic

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ABSTRACT

Background: LPV/r tablets compared to SGC have no oleic acid or sorbitol, have no refrigeration/food requirements, and have less pharmacokinetic variability. It was our objective to evaluate tolerability, quality of life (QoL), and lipid differences after switching from LPV/r SGC to Tablet.

Methods: Seventy-four HIV-infected subjects on LPV/r-based regimens were enrolled prior to (25/74) or within 8wks (49/74) after switching from LPV/r SGC to Tablet. Formulation preference and satisfaction were assessed post-switch. Tolerability assessments included bowel habit (BH), global condition improvement (GCI), and ACTG symptom distress module (ASDM). Tolerability, QoL, and fasting lipids pre-switch were compared to Wk4 and Wk12. Baseline QoL and BH were recalled for those subjects enrolled post-switch.

Results: At Wk4, more patients preferred LPV/r Tablet to SGC (74% vs. 8%) and satisfaction with the Tablet formulation was expressed. Significant improvement in BH was reported at Wk4 (mean change in BH-score: -0.281, p=0.002) and maintained through Wk12 (p=0.014). Overall LPV/r tolerability improved with the switch. At Wk4, 45% of subjects felt "better", 45% felt "about the same", 5% "worse", and 5% did not respond. These GCI-improvements were maintained through Wk12 (p<0.0001). Correlation was seen between the BH-score and GCI-improvement at Wk4 (p=0.017) and waned by Wk12. ASDM and QoL were unchanged at Wk4 and Wk12. Interestingly, a mean reduction in triglycerides of 33mg/dl (18%), unrelated to lipid-lowering therapy, was observed at Wk12 (n=33, p=0.035).

Conclusions: Switching from LPV/r SGC to Tablet resulted in significant improvement in gastrointestinal tolerability with a resulting positive impact on subjects' overall well being (GCI). QoL was maintained. The observed 18% reduction in triglyceride level deserves further evaluation.

BACKGROUND

- The new LPV/r 200/50 mg tablet formulation has been well received by clinicians and patients because of its reduced daily pill burden from six SGC to four tablets, lack of special food requirements needed to achieve desired plasma drug exposure, and its stability at room temperature, eliminating the need for refrigeration [1-2].

BACKGROUND CONTINUED

- Because the new tablet formulation lacks oleic acid [3], an excipient believed to contribute to gastrointestinal (GI) intolerance with the SGC, it has been speculated that the tolerability of LPV/r would improve with the use of the tablet form.
- In this study, a phase IV tolerability assessment was conducted in HIV-infected subjects who were switched from the SGC to the tablet formulation of LPV/r. Self-reported daily bowel habit, quality of life (QOL), and fasting lipid profile obtained prior to the switch were compared to similar data obtained 12-weeks post-formulation change.

METHODS

- This was a prospective cohort study that enrolled clinically stable HIV-infected subjects receiving LPV/r-based antiretroviral (ARV) regimen.

Screening

- HIV-subjects age ≥18 years
- Enrolled prior to, or within 8 weeks of formulation switch
- No CD4 cell count restriction
- No pregnancy/breastfeeding

Daily bowel movement habit was evaluated prior to switch and at weeks 4 & 12 using an instrument that assessed:

- ✓Frequency
- ✓Consistency
- ✓Volume
- ✓Presence of blood in stool

Intervention

- QOL instruments were administered prior to switch and weeks 4 & 12:
  - ✓MOS HIV health survey
  - ✓Global condition improvement questionnaire
  - ✓Medication satisfaction survey
  - ✓Therapy preference survey
  - ✓ACTG Symptom Distress Module (ASDM) – supplemented with two questions to assess symptoms related to nephrolithiasis
- Clinical labs monitored at baseline and at week 12:
  - ✓Fasting Lipid Profile
  - ✓HIV-RNA PCR
  - ✓CD4 T-cell counts

RESULTS

Table 1. Subject demographic data at study entry

	Study population (n = 74)
Male sex [No. (%)]	61 (82.43)
Race African American [No. (%)] White [No. (%)] Hispanic [No. (%)]	55 (74.32) 17 (22.97) 2 (2.70)
†On LPV/r tablet at entry No [No. (%)] Yes [No. (%)]	49 (66%) 25 (34%)
On anti-diarrheal drug No [No. (%)] Yes [No. (%)]	67 (92) 6 (8)
On lipid lowering drug No [No. (%)] Yes [No. (%)]	54 (74) 19 (26)
Median age [years (75% percentile)]	43 (39-47)
Median weight [Kg (75% percentile)]	80.5 (69.6-88.6)
Median HIV-1 RNA [copies/ml (75% percentile)]	0.135 (0.05-0.70)
Median CD4 T-cell counts [(cell/µl 75% percentile)]	294 (157-455)

LPV/r, lopinavir/ritonavir; SGC, soft gel capsule; †Subjects were already switched from LPV/r SGC to tablets within 8 weeks prior to enrollment; 75% percentile, 25th to 75th percentile.

Table 2: Quality of life assessment

Quality of life instruments	Baseline	Change (Baseline to Week 4)		Change (Baseline to Week 12)	
	Mean ± SD	Mean ± SD	P-value	Mean ± SD	P-value
MOS-HIV Physical Health Summary Score (PHS)	48.2 ± 11.5	0.015 ± 9.00	0.97	0.315 ± 9.20	0.79
MOS-HIV Mental Health Summary Score (MHS)	50.7 ± 12.0	0.366 ± 9.07	0.74	0.313 ± 10.01	0.81
ACTG Symptoms Distress Module (ASDM)	26.7 ± 19.8	-2.99 ± 16.34	0.14	-2.92 ± 16.48	0.17
Center for Epidemiology Studies-Depression (CES-D)	14.5 ± 10.2	-1.12 ± 8.00	0.25	-0.753 ± 8.47	0.49
		Mean (Week 4)		Mean (Week 12)	
Medication satisfaction survey (MSS)		9.01 ± 2.27	NA	8.69 ± 2.25	NA
Global Condition improvement (GCI)		2.24 ± 3.05	<0.0001	2.46 ± 3.30	<0.0001*
Therapy preference: Prefer LPV/r Tablet [No. (%)] Prefer LPV/r SGC [No. (%)] No preference [No. (%)]		55 (78%) 6 (9%) 9 (13%)	<0.0001	46 (74%) 6 (10%) 10 (16%)	<0.0001*

Quality of life instruments were scored according to the published scoring algorithm [4]; SD, standard deviation; SGC, soft gel capsule; LPV/r, lopinavir/ritonavir

Table 3: Change in self-reported bowel habit

Variables	Baseline to Week 4		Baseline to Week 12	
	Improvement rate	P-value	Improvement rate	P-value
Decrease in stool frequency among those reporting change	18/28 ± 64.3%	0.13	18/32 ± 56.3%	0.48
Improved stool consistency among those reporting change	23/30 ± 76.75%	0.0035	19/27 ± 70.4%	0.0343*
Decrease in stool volume among those reporting change	11/16 ± 68.8%	0.13	8/13 ± 61.5%	0.41
Resolution of blood in stool among those reporting change	5/6 ± 83.3%	0.10	4/6 ± 66.7%	0.41
	Baseline to Week 4 (n= 70)		Baseline to Week 12 (n=62)	
Overall change in bowel habit score (BHS) [mean ± SD]	-0.281 ± 0.719	0.0017	-0.227 ± 0.707	0.0141*

Self-reported bowel habit score (BHS) was assessed on a scale in which stool consistency was (solid =1, loose =3, watery=5); volume (small =1, moderate=3, large=5), blood (no=1, yes=5); Frequency (1 – 5). For example, a subject with baseline responses of: Solid, Moderate, no blood, and frequency of "2" would have a score of: (1 + 3 + 1 + 2)/4 = 1.75 for their baseline summary score. Therefore the scale has a minimum of 1 (best BHS outcome) and a maximum of 5 (worst BHS outcome); SD, standard deviation.

RESULTS CONTINUED

Table 4: Changes in Fasting Lipid Profile from Baseline to Week 12

	Lipid Lowering Drug	Baseline Mean (SD)	Week 12 Mean (SD)	Mean change (SD)	P-value
TC	No (n =38) Yes (n=16) Total population (n=54)	188 (35.1) 221 (66.2) 198 (48.4)	179 (34.7) 218 (55.8) 190 (45.3)	-9.20 (23.20) -2.94 (44.30) -7.33 (30.70)	0.0197* 0.795 0.0848
TRIG	No (n=33) Yes (n=14) Total population (n=47)	187 (117) 410 (410) 254 (260)	154 (111) 329 (304) 206 (203)	-33.10 (86.30) -81.20 (348.30) -47.40 (199.90)	0.035* 0.399 0.1108
HDL-C	No (n=33) Yes (n=14) Total population (n=47)	47.0 (11.3) 35.1 (15.9) 43.2 (14.0)	42.6 (11.9) 36.8 (15.8) 40.7 (13.4)	-4.50 (9.40) 1.70 (9.50) -2.49 (9.78)	0.012* 0.490 0.877
LDL-C	No (n=33) Yes (n=14) Total population (n=47)	106 (29.4) 123 (54.5) 111 (38.8)	102 (24.4) 127 (32.3) 110 (29.0)	-4.20 (21.80) 3.60 (48.60) -1.85 (31.80)	0.283 0.788 0.692

TC; total cholesterol; Trig, triglyceride; HDL-C, high density lipoprotein; LDL-C, low density lipoprotein; SD, standard deviation. *Statistically significant (P ≤ 0.05).

DISCUSION AND CONCLUSIONS

- At Week 4, more patients preferred LPV/r Tablet to SGC (74% vs. 8%) and satisfaction with the Tablet formulation was expressed. Significant improvement in bowel habit was reported at Week 4 (mean change in BH-score: -0.281, p=0.002) and maintained through Week 12 (p=0.014).
- Switching from LPV/r SGC to Tablet resulted in significant improvement in GI tolerability with a resulting positive impact on subjects' overall well being (GCI). Overall LPV/r tolerability improved with the switch. At Week 4, 45% of subjects felt "better", 45% felt "about the same", 5% "worse", and 5% did not respond. QoL was maintained (as measured by GCI-improvements) through Week 12 (p<0.0001). Correlation was seen between the BH-score and GCI-improvement at Week 4 (p=0.017) and waned by Week 12.
- There was not enough evidence to conclude a change in QOL due to the switch in drug formulation as measured by MOS-HIV PHS, MOS-HIV MHS, or ASDM scores (Table 2).
- Interestingly, a mean reduction in triglycerides of 33 mg/dL (18%), unrelated to lipid-lowering therapy, was observed at Week 12 (n=33, p=0.035). This reduction in triglyceride level deserves further evaluation.

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