

A Comparison of Adverse Events and Quality of Life Before and After Switching from Kaletra™ Soft-gel to Kaletra™ Tablets in an African American Cohort

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Background

- Lopinavir/ritonavir (LPV/r; Kaletra™) is a protease inhibitor (PI) formulated to take advantage of the high genetic barriers to resistance generally found in PIs. LPV/r, a co-formulation of the potent but rapidly metabolized PI lopinavir [(LPV); >10 times more potent than ritonavir (RTV)] and RTV, is specifically formulated to overcome many of the absorption, distribution, metabolism and excretion (ADME) limitations of early PIs while minimizing resistance and increasing tolerability. LPV/r possesses a unique PK profile and extremely high Inhibitory Quotient (IQ = C_{min}/IC₅₀ wt).^[1,2]
- LPV/r was available in a soft-gel capsule (SGC) and liquid formulation. Excipients of the SGC included oleic acid, which has been associated with diarrhea.^[3] A newly formulated tablet, approved in the US in October, 2005, is dosed at 4 tabs qd or 2 tabs BID.
- The hypothesis is that patients' quality of life will improve when switched from Kaletra™ soft-gel to tablet formulation by reducing pill count, eliminating food restrictions and the need to refrigerate the drug.



Methods

- This was a phase IV, open label, two-center prospective review comparing the acceptance and tolerability of Kaletra™ soft-gel capsules (800/200 mg) BID and Kaletra™ tablets (800/200 mg) BID.
- Subjects were monitored at week 4 and 12 weeks after the baseline visit at which time they switched to the tablet formulation. The objective was to compare patient preference, tolerability of the tablets and determine the proportion of patients achieving or maintaining viral load <400 and 50 copies/ml at week 12.
- Medication preference and adverse events including gastrointestinal side effects were assessed at each clinic visit.
- Thirty-one (31) subjects were enrolled in this study examining quality of life, tolerability and treatment preference prior to and following switch from soft-gel capsule formulation to tablets. Twenty-five (25) patients completed the study. Each were administered LPV/r on a BID schedule.

Key Entry Criteria

- Documented HIV Infection
- African-American male or female ≥18 years of age
- Currently on Kaletra™ Soft-gel capsules for >2 weeks
- No current gastrointestinal symptoms at baseline of Grade II or greater
- No recent illness in the preceding 30 days which in the opinion of the investigator would preclude inclusion in the study
- Competent and willingness to sign and date a written consent

Methods (continued)

Study Design and Analysis

Responding subjects were administered a series of questionnaires immediately prior to and 4 and 12 weeks following switch from soft-gel capsule to tablet formulation. These include:

Medical Outcomes Study – HIV (MOS-HIV) – a validated instrument assessing quality of life consisting of questions to assess physical, social, and emotional well being during the previous 4 weeks. Scores are standardized to a reference population with higher values representing better quality of life.^[4]

Center for Epidemiologic Studies – Depression (CES-D) – a 20 item questionnaire assessing factors consistent with a depressive state during the previous week.^[5] A score of 16 or higher indicates that the subject is experiencing symptoms of depression.

Modified Global Condition Improvement (GCI) – measures overall tolerability and HIV treatment preference.

Medication Satisfaction Survey – a 5 item questionnaire evaluating the patients experience with the formulation of Kaletra™ taken within the prior 4 weeks.

Therapy Preference Questionnaire – measures overall preference between the capsule and tablet formulation.

Statistical analysis was conducted using repeated measures (mixed model, or paired t-test or non-parametric test) for comparisons at baseline, week 4 and week 12 with 0.05 level of significance.

Table 1: Summary of Characteristics at Time of Formulation Switch

	n = 25	
Gender – n (%)		
Male	18	(72.0)
Female	7	(28.0)
Race/Ethnicity – n (%)		
African-American	25	(100.0)
Age – mean (range)	42	(23–56)
Therapy – n (%)		
First ARV	6	(24.0)
First PI	7	(28.0)
Third line	12	(48.0)
Average time – SGC (weeks) (range)	4–285	
mean	88	
median	64	
Viral load at time of switch – mean copies/mL (range)	5,042 (50–100,000)	
Patients – <400 copies/ml (%)	19	(76.0)
Patients – <50 copies/ml (%)	9	(36.0)
CD4+ at switch – cells/mm³ – mean (range)	392 (10–1,048)	
<50 cells/mm³ – n (%)	4	(16.0)

Results

General health perception includes degree of illness, perception of health compared to others, degree of agreement that health is “excellent”, and whether or not one has been feeling badly lately. Little or no changes were observed in quality of life, cognitive function, health transition, vitality, health distress scores, social function, physical health and mental health summary scores (e.g., perceived health compared to 4 weeks ago) (Table 2). Highest MOS-HIV score denotes improvement in all subscale categories below.

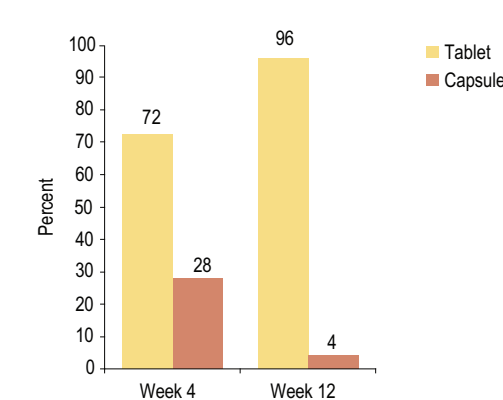
Post-formulation switch, demonstrates modest improvement in general health, mental health, and role function (Table 2).

Table 2: MOS-HIV Subscales and CES-D

	Baseline	Week 4
MOS-HIV		
Role Function	72	74
General Health	61	63
Health Transition	66	68
Pain	81	90
Quality of Life	69	66
Social Function	89	88
Cognitive Function	80	80
Vitality	68	70
Physical Health Summary Score	52	54
Mental Health Summary Score	53	52
Mental Health	77	79
Physical Function	80	84
Health Distress	80	79
CES-D	33.6	35.8

- Based on overall experience with Kaletra™ treatment, a vast majority preferred the tablet formulation.
- This trend strengthened between weeks 4 and 12 and is related to tablets not requiring refrigeration.

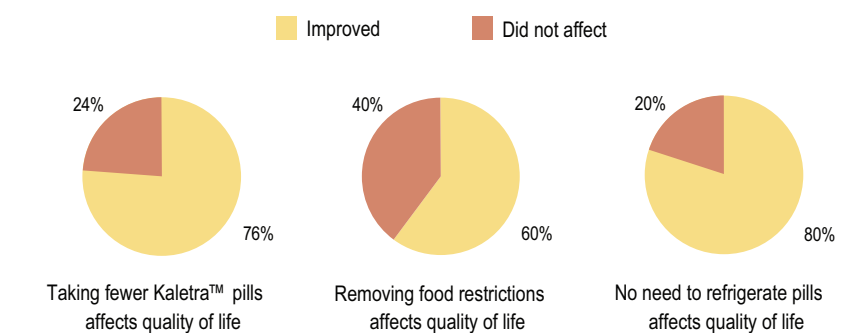
Figure 1: Therapy Preference Questionnaire Overall Experience



Results (continued)

Overall satisfaction with LPV/r therapy was very high with the vast majority of respondents indicating preference for tablet formulation (Figure 2).

Figure 2: Therapy Preference Questionnaire



Conclusions

- Following switch from LPV/r capsules to tablets, subjects reported:
 - the same or improved tolerability post switch (96% of subjects).
 - high preference for LPV/r tablet formulation citing no need for refrigeration as the primary reason.
- No significant change in lipids, triglycerides, liver function laboratory values or GI manifestations.
- Serum glucose suggests a decline from baseline – week 12, however this requires additional study in light of the sample size of this evaluation.
- Viral response rate, CD4 lymphocyte counts remained constant. No viral rebound noted post switch.
- No additional toxicities noted post switch to tablets.

References

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