Improvements in self-reported adherence and adverse effects with lopinavir/ritonavir after switching from soft-gel capsules (SGC) to Tablets varies by ethnicity

Poster P103

S Schrader[1], SK Chuck[2], LW Rahn[2], KG Emrich[2], PS Parekh[2]
[1]The Schrader Clinic, Houston, TX, USA,[2]Abbott Laboratories, Abbott Park, IL, USA

BACKGROUND

- Kaletra (lopinavir/ritonavir, LPV/r) Tablets were FDA approved in October 2005.
- Short-term results in HIV-negative, healthy volunteers suggest improved tolerability, but data in HIV-infected patients have not been previously reported.[Klein C, et al. *EACS*, 2005, PE4.3/2]
- Features of LPV/r Tablets compared to Soft Gel Capsule (SGC) [Kaletra US Prescribing Info. 10/05]
  - –Based on novel Melt-Extrusion technology
  - –No refrigeration
  - –Less pharmacokinetic variability
  - –Contains 200 mg of lopinavir and 50 mg of ritonavir
  - –Daily pill count decreased from 6 to 4 for same daily dose of 800/200 mg
  - -No oleic acid or sorbitol
  - -No need for dosing with food

OBJECTIVES

- To analyze ethnic differences in the following parameters based on patient self-report during the conversion of LPV/r SGC to Tablet formulations dosed 400/100mg twice a day
  - •Patient preference between LPV/r SGC and Tablet formulations
  - •Benefits
  - •Satisfaction
  - •Tolerability
  - •Adherence
  - -Missed doses, fewer pills
  - -Reasons for missed doses
  - –Overall, frequency & severity of select side effects
  - –Diarrhea & antidiarrheal use

METHODS – Survey Design

- Self-reported, anonymous, multiple-choice survey in English & Spanish
- Addresses satisfaction, overall tolerability, adverse effects, adherence, perceived benefits, formulation preference, and quality of life
- SGC and Tablets surveys had identical questions with 4 additional comparative questions (SGC vs. Tablets) in the Tablets survey
- Respondents were asked to think back over the last 4 weeks and indicate in a typical week the frequency & severity of side effects
- Adherence was reported by respondents based on the last week of dosing
- Questions written at grade 6 level

METHODS – Survey Distribution

- 52 out of 65 US physicians contacted distributed surveys to patients; a small payment to physicians were made for efforts related to distribution and handling of surveys with a maximum of 25 patients per site allowed; patients received no compensation
- Physicians provided surveys to the patients while on LPV/r SGC and LPV/r Tablets dosed at 400/100mg BID after a minimum of 4 weeks on each formulation.
- Patients completed the surveys in waiting area at their routine scheduled visits.
- Patient privacy was maintained by having patients seal completed surveys into envelopes prior to providing survey to clinic staff for mailing to research company managing the project.
- October 2005 through May 2006

DEMOGRAPHICS

- Surveys returned from 52 physicians in 20 states & Washington, DC
- 332 respondents were mostly males (85%) with diverse ethnicity.
- 87% of respondents were ≥ 35 years old.
- Duration of antiretroviral therapy
  - •59% at least 5 years
  - •31% 1 to 5 years
  - •10% < 1 year
- Duration of LPV/r therapy
  - •82% of LPV/r SGC experience was > 1 year
  - •89% of LPV/r Tablets experience was < 3 months

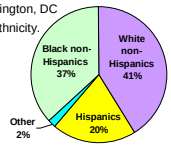
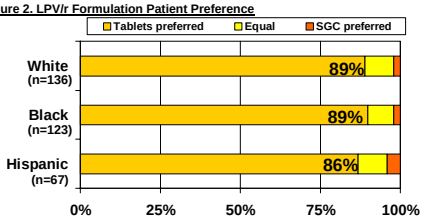


Figure 1. Ethnicity of Respondents

RESULTS

LPV/r Tablet formulation preferred over SGC by majority, regardless of ethnic group

Figure 2. LPV/r Formulation Patient Preference



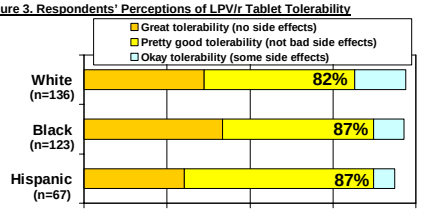
LPV/r Tablets benefits cited by respondents related to refrigeration, pill count, reduction in side effects, and food requirement

Table 1. LPV/r Tablet Benefits cited by Respondents

	White	Black	Hispanics
Not have to refrigerate	66%	71%	63%
It has fewer pills	64%	61%	55%
Does not give me bad side effects	47%	50%	40%
Not have to take with food	37%	49%	36%

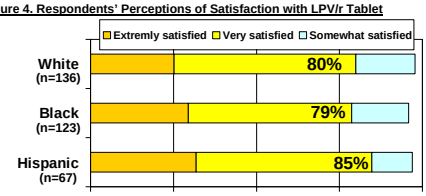
No differences across the ethnic groups were noted in **tolerability and satisfaction with LPV/r Tablets**

Figure 3. Respondents' Perceptions of LPV/r Tablet Tolerability



- Overall, 63% (SGC) vs. 84% (Tablets) of respondents had pretty good to great tolerability
- No respondents indicated bad tolerability (i.e., "terrible" side effects) on LPV/r Tablets

Figure 4. Respondents' Perceptions of Satisfaction with LPV/r Tablet



- Overall, 60% (SGC) vs. 80% (Tablets) of respondents were very or extremely satisfied
- Of 332 respondents, only 1 (Black) respondent indicated "not at all being satisfied" with LPV/r Tablets

RESULTS (continued)

For all ethnic groups, respondents had a significant improvements (p<0.05) in **diarrhea frequency and severity** after switching from LPV/r SGC to Tablets

- Overall, 82% of respondents reported no diarrhea or improvement in diarrhea
- Overall, an additional 21% of respondents indicated no or rare diarrhea (p<0.05)
- Overall, 76% of respondents reported no or rare antidiarrheal use (p<0.05)
- Antidiarrheal use decreased in all groups, with significant decreases observed in White non-Hispanics, the ethnic group reporting the highest rates of antidiarrheal use

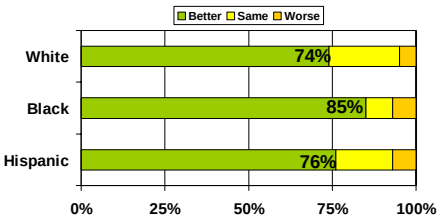
Table 2. Improvement in Antidiarrheal Use and Diarrhea Severity and Frequency

RELATIVE RISK (Tablets vs. SGC)	White (n=136)	Black (n=123)	Hispanic (n=67)
Antidiarrheal use (more than "rarely use")	0.72*	0.95	0.65
Diarrhea frequency 3+ per week	0.68*	0.52*	0.39*
Respondent self-defined "severe" diarrhea -Proportion of respondents (Tablets vs. SGC)	0.47* 7% vs. 15%*	0.13* 1% vs. 8%*	0.17* 2% vs. 12%*

*** indicates p<0.05**

All ethnic groups reported significant **improvement in side effects** with LPV/r Tablets

Figure 5. Improvement in Side Effects with LPV/r Tablets compared to SGC



- The greatest improvements were observed in Black non-Hispanics with 85% reporting side effect are better when switched from LPV/r SGC to Tablets (p<0.05)

Table 3. Significant Improvement in Gastrointestinal Side Effects by Ethnicity

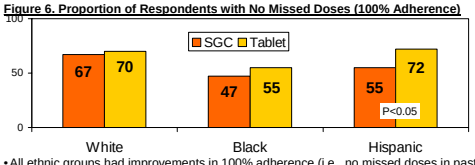
RELATIVE RISK with LPV/r Tablet vs. SGC	Race		
	White	Black	Hispanic
Diarrhea	Frequency 0.68 Severity 0.47	Frequency 0.52 Severity 0.13	Frequency 0.39 Severity 0.17
Nausea/Vomiting	Frequency 0.31		
Bloating/Gas	Frequency 0.54	Frequency 0.47 Severity 0.33	Frequency 0.41

Relative risk are noted for statistically significant(p<0.05) improvements in 1) severity - respondent self-defined "severe" severity, and 2) frequency – 3+ times per week

- Several GI side effects are improved with switching from LPV/r SGC to Tablets

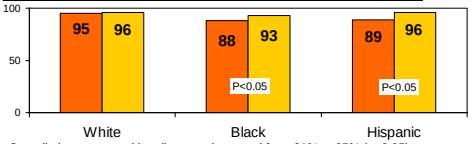
Self-reported adherence based on **missed doses** significantly improved after switching to LPV/r Tablets

Figure 6. Proportion of Respondents with No Missed Doses (100% Adherence)



- All ethnic groups had improvements in 100% adherence (i.e., no missed doses in past week) after switching from LPV/r SGC to Tablets; statistically significant for Hispanics

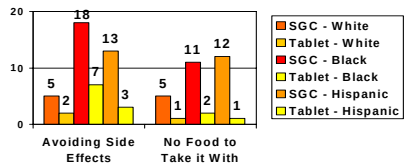
Figure 7. Mean Weekly Adherence based on Percentage of Doses Taken



- Overall, the mean weekly adherence improved from 91% to 95% (p<0.05)
- Black non-Hispanics reported lower adherence than White non-Hispanics on either LPV/r formulations (p<0.05); socioeconomic influences were not assessed
- For Black non-Hispanics and Hispanics the mean calculated weekly adherence significantly improved (both p<0.05)

Figure 8. Proportion indicating Reason for Missed Doses by Ethnicity

- Black non-Hispanics and Hispanics had significant decreases in missed doses due to avoiding side effects and not having food with them to take LPV/r (both p<0.05)



CONCLUSIONS

- In this survey of 332 HIV-infected US respondents, significant improvements were reported with switching from LPV/r SGC to Tablets dosed 400/100mg twice per day
  - LPV/r Tablets were preferred over SGC by ~9 in 10 respondents, regardless of ethnic group
  - No differences across the ethnic groups were noted in the significantly improved tolerability (82-87% had no/not bad side effects) and satisfaction (78-85% were very/extremely satisfied) with LPV/r Tablets
  - For all ethnic groups, respondents had a significant improvement (p<0.05) in diarrhea frequency and severity after switching from LPV/r SGC to Tablets
  - Some differences in improvements in nausea/vomiting and bloating/gas were observed by ethnic group
- The LPV/r Tablets benefit most frequently cited by respondents were related to refrigeration, pill count, reduction in side effects, and food requirement
- Significant improvement in adherence were seen in Black non-Hispanics and Hispanic respondents, closing the gap observed between ethnic groups with SGC
- These results suggest that LPV/r Tablets dosed BID provides multiple benefits to HIV infected patients relative to SGC for the ethnic groups studied. Additional study to further define the tolerability profile of LPV/r Tablets is warranted.

8th International Congress on Drug Therapy in HIV Infection, 12-16 November, 2006, Glasgow, UK

Abbott Virology