Significant improvements in self-reported gastrointestinal tolerability, quality of life, patient satisfaction, and adherence with lopinavir/ritonavir after switching from BID soft-gel capsule (SGC) to BID Tablets

Poster P104

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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 assess patient self-reported differences between LPV/r SGC and Tablet formulations when dosed twice daily (BID).
  - •Satisfaction
  - •Tolerability
  - •Overall
  - –Frequency & severity of select adverse effects
  - –Diarrhea & antidiarrheal use
  - • Adherence
  - - Missed doses, fewer pills
  - - Food requirement (SGC only)
  - - Reasons for missed doses
  - • Benefits & Quality of life
- To determine patient preference between LPV/r SGC and Tablet formulations when dosed BID.

METHODS – Survey Design

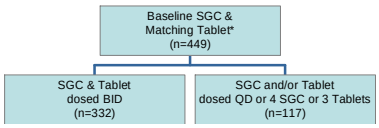
- Self-reported, anonymous, multiple-choice survey in English & Spanish
- Addresses satisfaction, overall tolerability, adverse effects, adherence, perceived benefits, formulation preference, and quality of life
- SGC and Tablet surveys had identical questions with 4 additional comparative questions (SGC vs. Tablets) in the Tablet 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

Figure 1. Dosing of LPV/r for Returned Surveys



- 332 matched Tablet surveys with LPV/r SGC and Tablets dosed BID were returned from 52 physicians in 20 states & Washington, DC
- 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 Tablet experience was < 3 mos

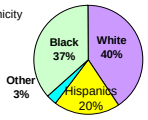
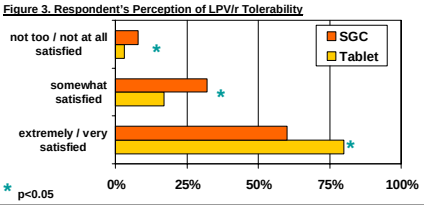


Figure 2. Ethnicity of Respondents

RESULTS

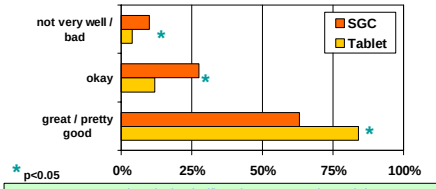
Significantly more respondents indicated they were **"extremely" or "very" satisfied** after switching to LPV/r Tablets (80% vs. 60% on SGC, p<0.05)

Figure 3. Respondent's Perception of LPV/r Tolerability



Significantly more respondents indicated **great" or "pretty good" tolerability** (i.e., no side effects or not bad side effects) after switching to LPV/r Tablets (84% vs. 63% on SGC, p<0.05)

Figure 4. Respondent's Perception of Satisfaction with LPV/r



Respondents had a significant improvements (p<0.05) in **diarrhea frequency and severity** after switching from LPV/r SGC to Tablets

- 82% reported no diarrhea or improvement
- An additional 21% more respondents indicated no or rare diarrhea (p<0.05)

Table 1. Improvement in Antidiarrheal Use, Diarrhea Severity and Frequency

	RELATIVE RISK (Tablets vs. SGC)
Antidiarrheal use (more than "rarely use")	0.73*
Diarrhea frequency 3+ per week	0.60*
Respondent self-defined "severe" diarrhea -Proportion of respondents	0.28* 3.3% vs. 11.7%*

* p<0.05

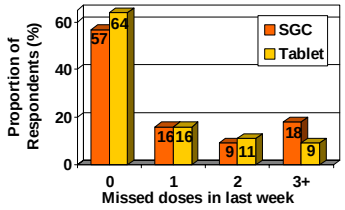
RESULTS (continued)

Significantly fewer respondents reported **bloating, gas, or pain in stomach**, and those who did had diminished frequency on LPV/r Tablets

- An additional 12% more respondents indicated no or rare occurrence (p<0.05)
- Only 5% reported "severe" episodes (vs. 8% for SCG, p<0.10)

Self-reported adherence based on **missed doses** significantly improved after switching to LPV/r Tablets (95% vs. 91% for SGC, p<0.05)

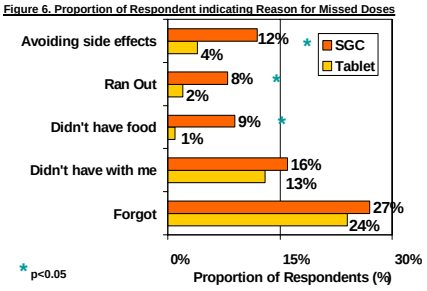
Figure 5. Proportion of Respondent Missing LPV/r Doses



- An additional 7% of respondents reported no missed doses with LPV/r Tablets

Significant improvements were observed in 3 **reasons for non-adherence** after switching to LPV/r Tablets; avoiding side effects, running out, and not having food with them to take with the LPV/r dose

Figure 6. Proportion of Respondent indicating Reason for Missed Doses



LPV/r Tablet benefits cited by respondents related to refrigeration, pill count, and food requirement

- Respondents cited the following as benefits they "liked"
  - •Don't have to refrigerate (67%)
  - •Fewer pills (61%)
  - •Don't have to take with food (41%)
- 41% of respondents cited the lack of dietary restriction as a benefit. This may be explained by the similar level of non-adherence to LPV/r SGC's food requirement.
  - •44% of respondents indicated at least 1 dose of LPV/r SGC was taken without food in the last week
  - •An average of 16% of LPV/r SGC doses were taken without food

LPV/r Tablet was the **preferred formulation** over SGC by 88% of respondents, with 79% of respondents stating that side effects were better with LPV/r Tablet

Figure 7. Formulation Preference

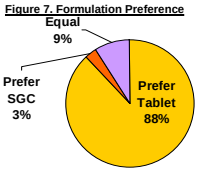
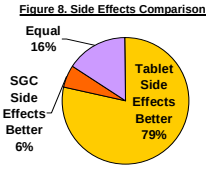
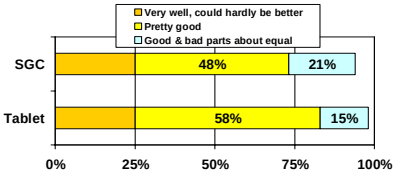


Figure 8. Side Effects Comparison



Quality of life over the last 4 weeks improved after switching to LPV/r Tablets

Figure 7. Respondent's Perception of Quality of Life Ratings



- Significant improvements in quality of life ratings were observed with a shift from "good & bad parts about equal" to "pretty good" quality of life (p<0.05)
- Quality of life improvements were noted by 73% and worsening by 2% of respondents when switched LPV/r Tablets

CONCLUSIONS

In this US survey of 332 HIV-infected patients, significant improvements were reported by patients switching from LPV/r SGC dosed BID to Tablets dosed BID.

- •82% of respondents reported no or improved diarrhea
- •Additional 12% of respondents reported no or rare bloating, pain, gas in stomach
- •Significant improvements in satisfaction, as well as overall tolerability, for ~20% of respondents
- •Adherence improved from 91% to 95%, with additional 7% of respondents reporting no missed doses

The LPV/r Tablet benefit most frequently cited by respondents were

- •Don't have to refrigerate (67%), fewer pills (61%), don't have to take with food (41%)

These results suggest that LPV/r Tablets dosed BID provides multiple benefits to HIV patients relative to SGC. Additional study to further define the tolerab… Tablets is warranted.

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

Abbott Virology