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

Poster # 81

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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 oleic acid or sorbitol
  - –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 refrigeration
  - –No need for dosing with food
  - –Less pharmacokinetic variability

OBJECTIVES

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

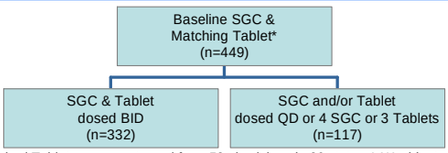
METHODS – Survey Design

- 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 on based on the last week of dosing
- Questions written at grade 6 level

METHODS – Survey Distribution

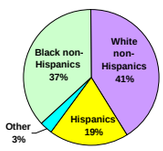
- 52 out of 65 US physicians contacted distributed surveys to patients; a small payment to physicians were made for efforts related to distribution and handling of surveys with a maximum of 25 patients per site allowed; patients received no compensation
- Physicians provided surveys to the patients while 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



* Matched Tablet surveys returned from 52 physicians in 20 states & Washington, DC

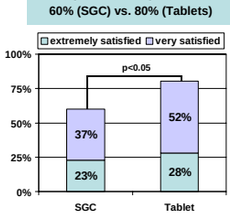
- 332 respondents were mostly males (85%) with diverse ethnicity.
- Majority of respondents were ≥ 35 years old.
  - •46% were > 45 years old
  - •41% were 35-44 years old
  - •13% were < 35 years old
- Duration of antiretroviral therapy
  - •59% at least 5 years
  - •31% 1 to 5 years
  - •10% < 1 year
- Duration of LPV/r therapy
  - •82% of LPV/r SGC experience was > 1 year
  - •89% of LPV/r Tablet experience was < 3 months



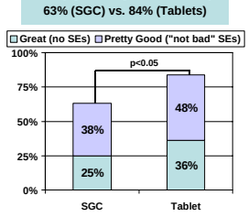
RESULTS

84% of respondents indicated **"pretty good" or "great" tolerability** after switching to LPV/r Tablets dosed BID; 21% more than with SGC (p<0.05)

SATISFACTION
Very or extremely satisfied
60% (SGC) vs. 80% (Tablets)



TOLERABILITY
Pretty good or great tolerability
63% (SGC) vs. 84% (Tablets)



- SE = side effects

Respondents had a significant improvement in **diarrhea** after switching to LPV/r Tablets

- 82% reported no diarrhea or improvement
- 21% more respondents indicated no or rare diarrhea (p<0.05)
- Only 3% reported "severe" diarrhea (vs. 12% for SGC, p<0.05)
- Antidiarrheal use of 3+ times per week was reduced by half (p<0.05)
- 76% of respondents reported no or rare antidiarrheal use (p<0.05)

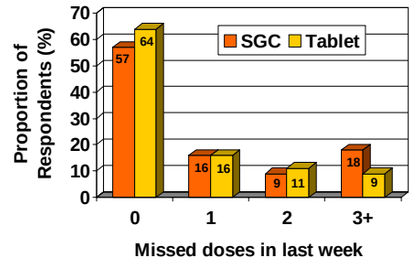
RESULTS (continued)

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

- 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

- Mean number of missed doses per wk decreased (from 1.25 to 0.71, p<0.05)
  - –this is equivalent to adherence improving from 91% to 95%
- More respondents indicated "not missing doses" (i.e. 100% of doses were taken) in the last week after switching to Tablets
  - –Yes/no response 52% vs. 60%, p<0.05
  - –Zero missed doses response 57% vs. 64%, p<0.10



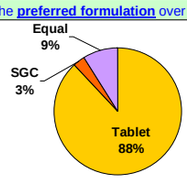
Significant improvements were observed in 3 **reasons for non-adherence** after switching to LPV/r Tablets

*** p<0.05**

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

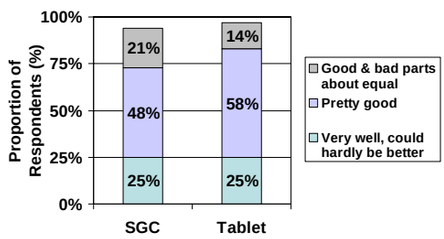
- Respondents cited the following as benefits they "liked"
  - •Don't have to refrigerate (67%)
  - •Fewer pills (61%)
  - •Don't have to take with food (41%)
- 41% of respondents cited the lack of dietary restriction as a benefit. This may be explained by the similar level of non-adherence to LPV/r 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



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

- 73% improved and 2% worsened with Tablets compared to SGC
  - •Significant improvements in quality of life were observed with a shift from "good & bad parts about equal" to "pretty good" quality of life (p<0.05)



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
- •12% more 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 7% more 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 tolerability profile of LPV/r Tablets is warranted.

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Abbott Virology