Switching to lopinavir/ritonavir (LPV/r) Tablets once daily (TAB-QD) from soft-gel capsule dosed BID/QD (SGC-BID/SGC-QD) led to significant improvements in tolerability, diarrhea, antidiarrheal medication use, and satisfaction

Poster # 83

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]
- Compared to twice daily (BID) dosing, once daily (QD) dosing of LPV/r Soft Gel Capsule (SGC) was associated with an increased rate of Grade 3+ diarrhea from 5% vs. 16%. [Johnson MA, et al. JAIDS. 2006]
- 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 dosed BID (SGC-BID) or QD (SGC-QD) and LPV/r Tablet formulation dosed QD (TAB-QD).
  - •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-BID or SGC-QD and LPV/r TAB-QD.

METHODS – Survey Design

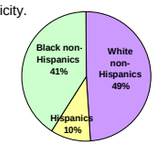
- Self-reported, anonymous, multiple-choice survey in English & Spanish
- Addresses satisfaction, overall tolerability, adverse effects, adherence, perceived benefits, formulation preference, and quality of life
- SGC and Tablet surveys had identical questions with 4 additional comparative questions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

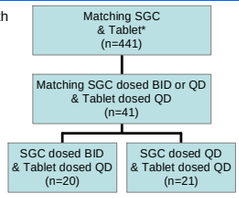
METHODS – Survey Distribution

- 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

- The 41 respondents were mostly males (76%) with diverse ethnicity.



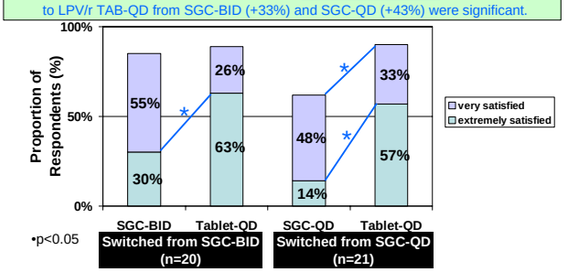


* Matched Tablet surveys returned from 52 physicians in 20 states & Washington, DC

- Majority of respondents were > 35 years old.
  - •> 45yrs (34%), 35-44yrs (39%), < 35yrs (27%)
- Duration of antiretroviral therapy
  - •≥ 5yrs (41%), 1-5yrs (49%) , < 1yr (10%)
  - •The SGC-BID and SGC-QD groups had similar durations of therapy.
- Duration of LPV/r therapy
  - •> 1 year LPV/r SGC (80%) and <3 months LPV/r Tablet (81%)

RESULTS

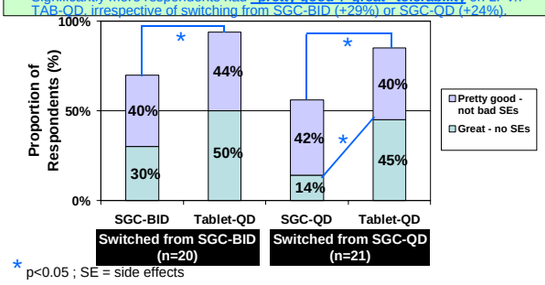
Increases in the proportion of respondents **"extremely" satisfied** after switching to LPV/r TAB-QD from SGC-BID (+33%) and SGC-QD (+43%) were significant.



•p<0.05

- A similar proportion of respondents were "extremely" satisfied with TAB-QD, independent of switching from SGC-BID (63%) or SGC-QD (57%).
- Overall 90% of respondents (n=41) were "very" or "extremely" satisfied on Tablets dosed QD (vs. 73% on SGC).

Significantly more respondents had **"pretty good"/"great" tolerability** on LPV/r TAB-QD, irrespective of switching from SGC-BID (+29%) or SGC-QD (+24%).



* p<0.05 ; SE = side effects

- Overall 90% of respondents (n=41) felt they had "pretty good" or "great" tolerability on Tablets dosed QD (vs. 64% on SGC).
- Greater improvements were noted when switching from SGC-QD vs. SGC-BID.

RESULTS (continued)

Respondents had improvements in **diarrhea** prevalence, severity & antidiarrheal use after switching to LPV/r Tablets dosed QD

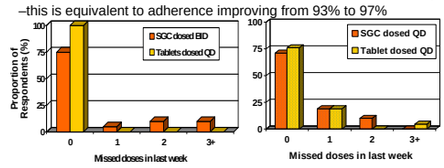
- Overall, 78% reported no diarrhea or had improvements in diarrhea
  - •Improvements were greater when switched from SGC-QD vs. SGC-BID
- Proportion of respondents reporting no diarrhea after switch to TAB-QD
  - •SGC-BID (n=20): doubled (p<0.10)
  - •SGC-QD (n=21): more than quadrupled (p<0.05)
- No reports of "severe" diarrhea on TAB-QD (vs. 8% for SGC, p<0.10)
- Antidiarrheal use of 1+ times per wk decreased from 44% to 20% (p<0.05)
  - •80% of respondents indicated no or rare antidiarrheal use (vs. 56% for SGC)

Bloating, pain, or gas in stomach & nausea were decreased with no "severe" episodes on LPV/r Tablets dosed QD

- Bloating, pain, or gas in stomach prevalence decreased and those who experienced episodes had diminished frequency on Tablets dosed QD
- Nausea prevalence decreased from 27% to 5% (p<0.05)

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

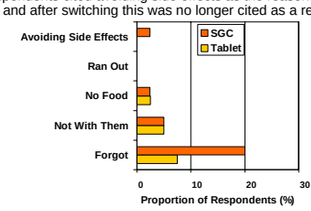
- Mean number of missed doses per week decreased (from 0.49 to 0.24)
  - –this is equivalent to adherence improving from 93% to 97%



- More respondents (n=41) indicated "not missing doses" (i.e. 100% of doses were taken) in the last week after switching to TAB-QD when measured with yes/no response (+10%) or indicating the number of missed doses (+20%)
  - –75% on SGC-BID vs. 90% on TAB-QD reported no missed doses

Forgetting doses decreased when switching from either LPV/r SGC-BID or SGC-QD to Tablets dosed QD

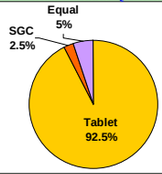
- 5% of respondents cited avoiding side effects as the reason for missing doses on SGC-QD and after switching this was no longer cited as a reason.



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

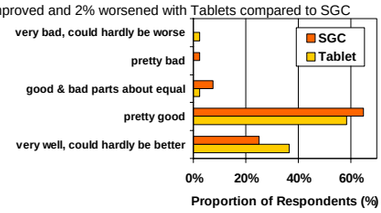
- Respondents cited the following as benefits they "liked"
  - •I can take it just once a day (75%)
  - •I take fewer pills (73%)
  - •I don't have to take it with food (68%)
  - •I don't have to refrigerate it (65%)
- 68% of respondents cited the lack of dietary restriction as a benefit. This is only partially explained by the 34% of respondents non-adherence to LPV/r SGC's food requirement.
  - •34% of respondents indicated at least 1 dose of LPV/r SGC was taken without food in the last week
  - •On average of 17% (1.6/7) of QD doses and 22% (2.4/14) of BID doses of LPV/r SGC were taken without food.

The **preferred formulation** by 93% of respondents was LPV/r Tablets dosed QD over SGC



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

- 73% improved and 2% worsened with Tablets compared to SGC



CONCLUSIONS

In this US survey of 41 HIV-infected patients, significant improvements were reported after switching from LPV/r SGC dosed BID/QD to Tablets dosed QD.

- •80% of respondents indicated no or rare antidiarrheal use
- •Differences in GI side effects seen with SGC dosed QD vs. BID appear to be lessened with the LPV/r Tablet formulation
- •Significant improvements in satisfaction for 38% of respondents
- •Significant improvements in overall tolerability for 25% of respondents
- •Adherence improved from 93% to 97% and 15% more respondents had no missed doses after switching from SGC-BID to Tablets dosed QD

The LPV/r Tablet benefits most often cited by respondents were:

- •I can take it just once a day (75%), I take fewer pills (73%), I don't have to take it with food (68%), I don't have to refrigerate it (65%)

These results suggest that LPV/r Tablets dosed QD provides multiple benefits relative to SGC with patients valuing QD, fewer pills, and no food or refrigeration requirements. Additional assessments of QD dosing of LPV/r Tablet's tolerability profile are warranted.

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Abbott Virology