The StARS Study of Once Daily Atazanavir, Low-Dose Ritonavir, and Saquinavir: Impact of Changing LPVr to ATVr in Combination with SQV

48 Week Efficacy and Safety Results

AE Colson[1], CJ Cohen[1], K McLaughlin[1], A Habel[1], JA Hellinger[2]

[1]Community Research Initiative of New England, Boston, MA; [2]Tufts-New England Medical Center, Boston, MA

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BACKGROUND

- Atazanavir/ritonavir (300/100 mg once daily) and lopinavir/ritonavir (400/100 mg twice daily) have comparable efficacy in protease-inhibitor experienced patients (BMS 045 Study, Johnson, 2006).
- Atazanavir acts as a second booster for saquinavir (Boffito, 2006).
- Compared to other protease inhibitors, atazanavir has less effect on plasma lipid profiles, even with ritonavir boosting (Swainston, 2005).

HYPOTHESES

- Patients with sustained virologic suppression on a dual boosted PI regimen containing LPV/r and SQV will maintain suppression after LPV/r/SQV is changed to ATV/SQV/r
- The plasma lipid profile will improve after LPV/r/SQV is changed to ATV/SQV/r
- Visceral adiposity tissue (VAT) will improve after LPV/r/SQV is changed to ATV/SQV/r.

METHODS

Design: 48 week, open label, single arm study

Subjects: 12 adults with viral load suppression (by ultrasensitive assay) on a dual boosted PI regimen containing saquinavir and lopinavir/r (alone or in combination with nucleoside reverse transcriptase inhibitors) for at least 12 weeks

Intervention:

- At enrollment, all subjects changed from BID saquinavir and lopinavir/r to saquinavir hard-gel capsules 1200 mg QD, atazanavir 300 mg QD, and ritonavir 100 mg QD.
- Nucleoside reverse transcriptase inhibitors, if present, were continued.
- After 2 weeks, the saquinavir dose was increased to 1600 mg QD.
- Between week 24 and 48, the saquinavir dose was decreased to 1500 mg QD due to re-formulation of the drug.

Measurements:

- HIV RNA
- CD4 count
- Fasting lipid profile
- Trough LPV and SQV levels at baseline
- Trough ATV and SQV levels after an observed dose at both SQV doses
- CT scans done at baseline and week 48

Analyses: Proportions with sustained virologic suppression at weeks 24 and 48 were calculated with a 95% confidence interval. The nonparametric Wilcoxon signed rank test (Wilcoxon, 1945) was used to analyze change from baseline to weeks 24 and 48 in triglycerides, HDL, LDL total cholesterol, VAT, CD4 and CD4 percent. Because of the number of comparisons performed, a p-value of 0.005 was used for statistical significance

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RESULTS

Baseline Characteristics n=12

Characteristic	Value
Female (%)	2 (17)
Race (%) -Caucasian -African American	 9 (75) 3 (25)
Median age in years (range)	46 (37-60)
Median CD4 cell count per mm3 (range)	500 (168-1258)
Median total cholesterol in mg/dl (range)	220 (164-264)
Median triglycerides level in mg/dl (range)	252 (86-672)
Median LDL in mg/dl (range)	94 (41-143)
Median HDL in mg/dl (range)	42 (32-90)
Median VAT area on abdominal CT in cm2 (range)	131.2 (32.5-249.8)
Number of participants on each NRTI combination (%) -No NRTIs -1 NRTI -2 NRTIs -3 NRTIs	 6 (50) 1 (8.3) 4 (33.3) 1 (8.3)

Disposition

One subject withdrew from the study at week 12 due to pregnancy; her viral load was suppressed at the time of withdrawal.

Virologic and Immunologic Results

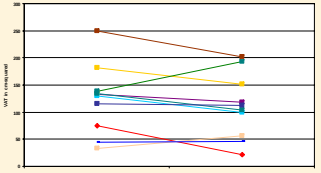
Week	% with viral load < 50 (95% CI)	CD4	CD4%*
12 (n=12)	100% (75-100)	500	31
24 (n=11)	100% (73-100)	426	35
48 (n=11)	100% (73-100)	502	35

Pharmacokinetic Results

	Week 2 SQV 1200 mg QD	Week 4 SQV 1600 mg QD	Target Trough
Median SQV trough ng/ml	256	222	100-250
Median ATV trough ng/ml	682	660	100

Abdominal CT and Lipid Results

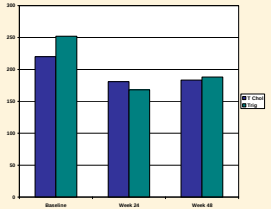
Change in Visceral Adipose Tissue



Median Visceral Adipose Tissue on a single slice abdominal CT trended down from 131.2 cm^2 at baseline to 108.6 cm^2 at week 48 (p>.2).

There was a significant decline in median total cholesterol from 220 at baseline to 183 at week 48 (p< 0.001) and a downward trend in median triglycerides from 252 at baseline to 188 at week 48 (p=0.18)

Change In T Chol and Trig



CONCLUSIONS

In this pilot study, patients suppressed on LPV/r and SQV (with or without NRTIs) substituted ATVr for LPVr and changed twice daily SQV to once daily SQV (dose range 1200-1600 mg). At week 48

- 100% of participants maintained virologic suppression on an ultrasensitive assay
- There was a significant decline in total cholesterol from 220 at baseline to 183 at week 48 (p<0.001)
- There was a downward trend in median triglyceride level from 252 at baseline to 188 at week 48
- There was a downward trend in visceral adiposity, as measured by single slice abdominal CT

The metabolic benefits of changing LPVr to ATVr in combination with SQV merit further study

REFERENCES: Johnson M et. al. AIDS 2006 March 21; 20 (5): 711-718; Swainston H et al. Drugs 2005 65 (16): 2309-2336; Boffito M et. al. AIDS Res Hum Retroviruses 2006 Aug; 22 (8): 749-56; Wilcoxon, F. (1945). "Individual comparisons by ranking methods." Biometrics Bulletin 1: 80-83.