



University of
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RESULTS OF SIMPLIFIED PROTEASE INHIBITOR TRIAL (SPRINT): ANTIVIRAL EFFECT OF ONCE DAILY SAQUINAVIR SGC PLUS RITONAVIR (SQV/r) vs TWICE DAILY INDINAVIR PLUS RITONAVIR (IDV/r)

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ABSTRACT

Background: IDV/r has been compared in a randomized clinical trial to twice daily SQV/r [MaxCmint Trial, JID 2003], but not to once daily SQV/r. SPRINT was a prospective, randomized, open-label trial comparing once daily SQV/r to twice daily IDV/r, each with 2 reverse transcriptase inhibitors (RTIs), with respect to proportions of patients with plasma viral load (VL) <50 copies/mL at 24 and 48 weeks.

Methods: 164 HIV+ adults were randomized to receive either SQV/r 1600 mg/ 100 mg once daily or IDV/r 800 mg/ 100 mg twice daily, with either 2 NRTIs or 1 NRTI plus 1 NNRTI as selected by the treating physician. Eligible patients had VL>5000 copies/mL and were either protease inhibitor (PI) naive, or had no evidence of PI resistance. VL, CD4, safety labs, and fasting lipids and glucose were assessed at screening and weeks 0, 4, 8, 12, 16, 24, 36 and 48. Follow-up was completed in March 2004. Categorical variables were compared between groups using the Chi-square test or Fisher's Exact Test, as appropriate. Continuous variables were compared using the Wilcoxon Rank Sum Test. Proportions were analysed using the Binomial test for two proportions. VL>5.0 log₁₀ copies/mL were set to 5.0.

Results: 147 evaluable patients were included in the efficacy analysis. At baseline, the SQV/r (n=70) and IDV/r (n=77) groups were similar (p>0.05) with respect to the following characteristics: median age 40 years, 79% male, 90% PI naive, 62% VL >5.0 log₁₀ copies/mL, median CD4 130 cells/mm³. Background regimens included an NNRTI in 3 patients on IDV/r and 0 on SQV/r. The SQV/r and IDV/r arms did not differ with respect to proportions of patients with VL<50 copies/mL by intent-to-treat analysis at either week 24 (56%, 49%, p=0.44) or week 48 (50%, 45%, p=0.70). CD4 increases to week 48 were also similar between arms (SQV/r 147 cells/mm³, p=0.60). However, 29/77 (38%) patients discontinued IDV/r by week 48 due to adverse events, mainly renal or gastrointestinal, as compared to 10/70 (14%) who discontinued SQV/r (p<0.01; 95% CI from IDV/r > by 8% to IDV/r > by 38%). No differences were observed between arms with respect to changes in fasting lipids or glucose from baseline to either week 24 or 48 (n=89, p>0.1).

Conclusions: In patients with PI-susceptible HIV, once daily SQV/r and twice daily IDV/r, each with 2 RTIs, are equally effective in achieving VL<50 copies/mL at 24 and 48 weeks, and have similar effects on fasting lipids and glucose. However, the IDV/r arm had a higher rate of discontinuation due to adverse effects.

OBJECTIVE

To compare once-daily SQV/r with twice-daily IDV/r, each with 2 RTIs, with respect to proportions of patients with plasma viral load (pVL) <50 copies/mL after 24 and 48 weeks

METHODS

STUDY DESIGN

- Open-label, multicentre trial
- 164 HIV positive adults
- Randomized 1:1 to receive either:
 - SQV 1600 mg/RTV 100 mg daily, or
 - IDV 800 mg/RTV 100 mg twice daily
- Plus 2 RTIs selected by treating physician

ENTRY CRITERIA

- Plasma VL ≥ 5000 copies/mL
- Either PI naive, or if PI experienced, no pVL rebound >1000 copies/mL while on PIs (unless genotype or phenotype taken at that time shows no PI resistance)
- The analysis includes 147 patients who were eligible and evaluable

LABORATORY ASSESSMENTS

At weeks 0, 4, 8, 12, 16, 24, 36, and 48

- Plasma viral load
- CD4 cell count and fraction
- Fasting glucose
- Fasting lipids
 - Total cholesterol (TC)
 - HDL cholesterol
 - LDL cholesterol
 - Triglycerides

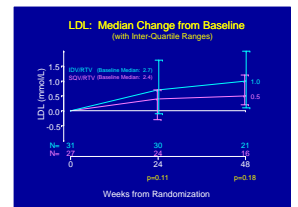
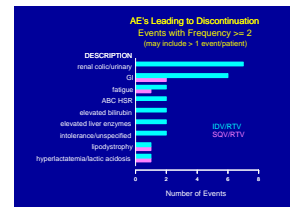
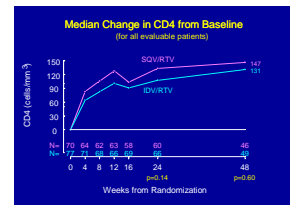
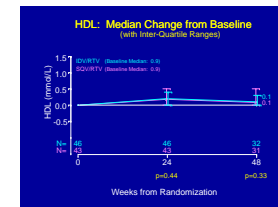
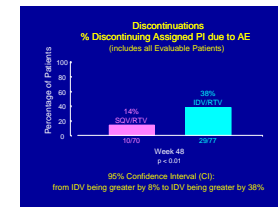
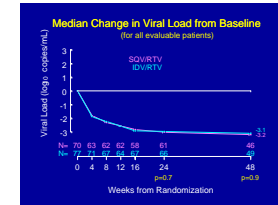
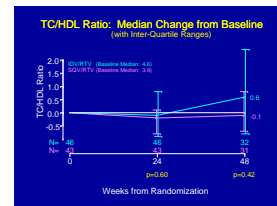
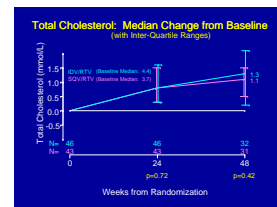
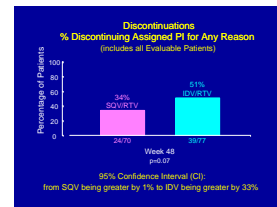
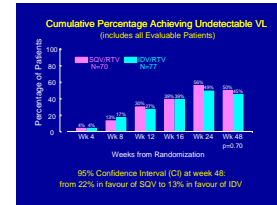
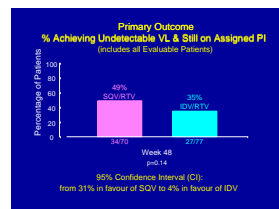
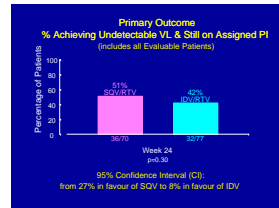
STATISTICAL ANALYSIS

- Categorical variables were compared between groups using the Chi-square Test or Fisher's Exact Test, as appropriate.
- For continuous variables, medians and inter-quartile ranges were calculated and comparisons made using the Wilcoxon Rank Sum Test, due to deviations from the Normal distribution in many cases.
- P values > 0.05 are considered not significant (NS).
- All pVL results >100,000 copies/mL were set to 100,000 (5.0 log₁₀) copies/mL for the analysis.

RESULTS

Baseline Characteristics

	SQV/r	IDV/r	P
N	70	77	
%Male	77%	88%	NS
%PI-naïve	40	41	NS
%PI-experienced	91%	93%	NS
%DU	22%	18%	NS
CD4 (cells/mm ³), med	152	122	NS
pVL (log ₁₀ copies/mL), med	5.0	NS	



CONCLUSIONS

In patients with PI-susceptible HIV, once-daily SQV/r and twice-daily IDV/r, each with 2 RTIs, are equally effective in achieving viral load <50 copies/mL at 24 and 48 weeks, and have similar effects on fasting lipids and glucose. However, the IDV/r arm had a higher rate of discontinuation due to adverse effects, mainly renal or gastrointestinal.

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