



# Durability of Ritonavir (RTV) Plus Saquinavir (SQV) Dual Protease Inhibitor Therapy in HIV Infection: Five-Year Follow-up

Poster 550-T

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## STUDY OVERVIEW

### Study Design

- Open-label, multicenter, randomized study of four RTV/SQV dose regimens (400/400 BID, 600/400 BID, 400/400 TID, 600/600 BID) with specific criteria for treatment intensification with RTIs
- Inclusion criteria: HIV+, CD4+ 100-500 cells/mm<sup>3</sup>, PI-naïve
- Cross-Sectional Body Composition Survey beginning at Week 144

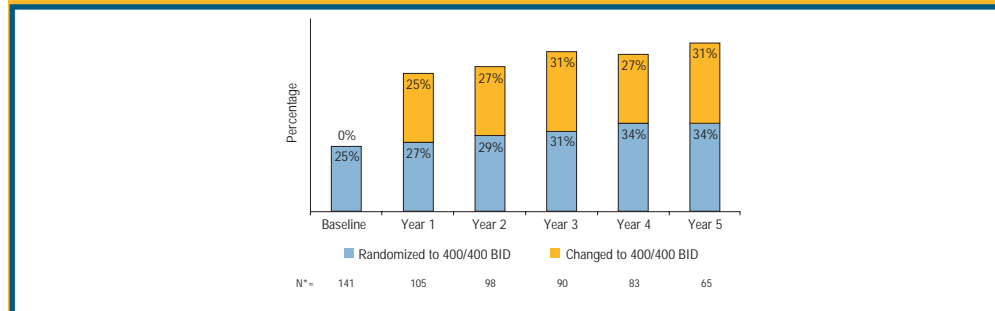
### Criteria for Treatment Intensification with RTIs

- HIV RNA >200 copies/mL at 12 weeks
- HIV RNA <200 copies/mL and then rebounded as demonstrated by two consecutive HIV RNA measurements >200 copies/mL
- HIV RNA decrease of at least 1.0 log<sub>10</sub> copies/mL from baseline and subsequently rebounded as demonstrated by two consecutive measurements within 1.0 log<sub>10</sub> copies/mL of baseline

After Week 48, subjects were allowed to add RTIs at the discretion of the investigators.

## RESULTS

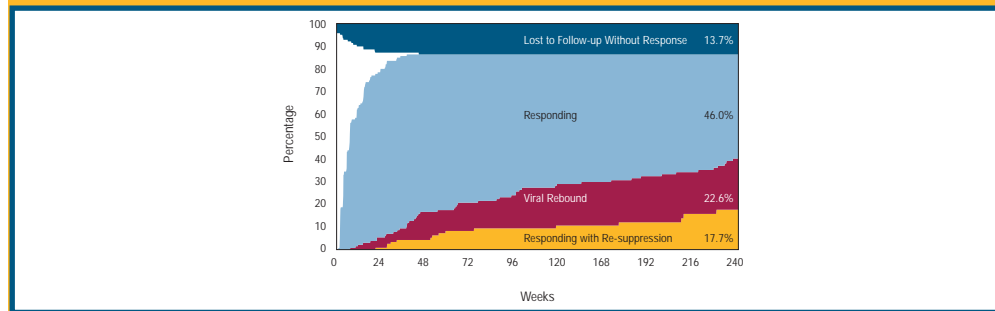
### Subjects on Ritonavir/Saquinavir 400/400 mg BID



### Evaluation of Response

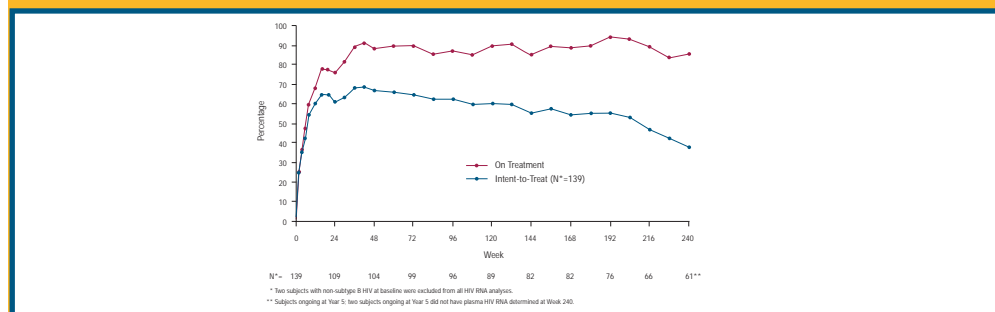
- All efficacy results are through 5 years of treatment
- Kaplan-Meier estimates
  - Time to initial viral response (<200 copies/mL)
  - Time to viral rebound (>200 copies/mL at two consecutive timepoints) after initial response
  - Time to subsequent viral re-suppression
- Percentage of subjects with plasma HIV RNA levels below 200 copies/mL
- Median CD4+ change over time

### Kaplan-Meier Analysis

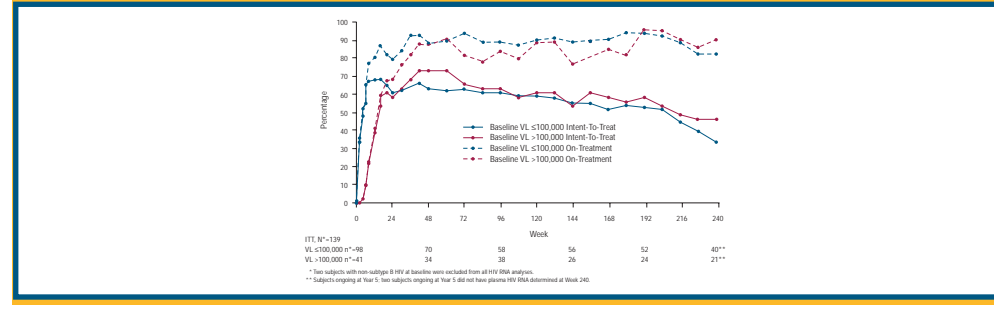


Results from the Kaplan-Meier analysis illustrate the tempo and cumulative rate of subjects that prematurely discontinued the study without experiencing a virologic response to antiretroviral treatment with RTV/SQV dual protease inhibitor therapy (13.7%). Of the 139 subjects included in this analysis, 120 (86.3%) experienced a virologic response. Of the 120 subjects experiencing virologic response, 64 (53.3%) achieved and maintained suppression of plasma viremia for approximately 5 years on antiretroviral treatment including RTV/SQV, while 56 (46.7%) experienced a virologic rebound during this time period. Of the 56 subjects that experienced virologic rebound, 25 (44.6%) subsequently achieved and maintained suppression of plasma viremia through Year 5, following treatment intensification with reverse transcriptase inhibitor therapy.

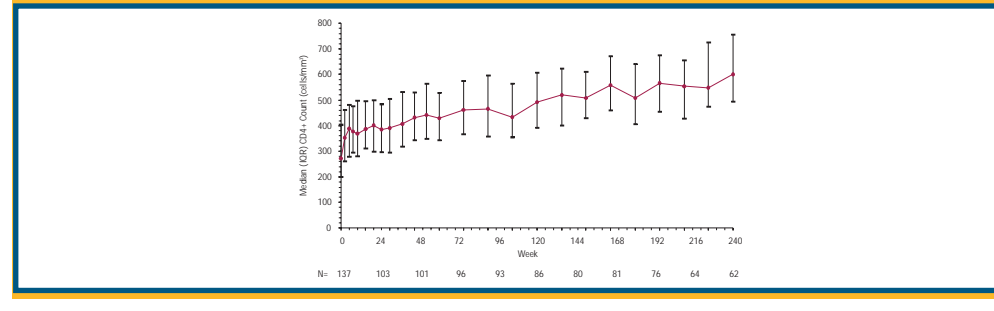
### HIV RNA <200 copies/mL



### HIV RNA <200 copies/mL by Baseline Viral Load



### CD4+ Cell Count (cells/mm<sup>3</sup>) Over Time



### Safety and Tolerability\*

| Adverse Event          | Year 1** (n = 141) | Year 2-3 (n = 106) <sup>†</sup> | Year 4-5 (n = 90) |
|------------------------|--------------------|---------------------------------|-------------------|
| Diarrhea               | 32 (23%)           | 9 (8%)                          | 7 (8%)            |
| Nausea                 | 26 (18%)           | 3 (3%)                          | 2 (2%)            |
| Asthenia               | 23 (16%)           | 10 (9%)                         | 4 (4%)            |
| Dizziness              | 12 (9%)            | 0 (0%)                          | 1 (1%)            |
| Vomiting               | 10 (7%)            | 1 (1%)                          | 0 (0%)            |
| Depression             | 10 (7%)            | 6 (6%)                          | 2 (2%)            |
| Circumoral Paresthesia | 10 (7%)            | 1 (1%)                          | 2 (2%)            |
| Peripheral Paresthesia | 8 (6%)             | 1 (1%)                          | 0 (0%)            |
| Taste Perversion       | 7 (5%)             | 0 (0%)                          | 1 (1%)            |

\* Most common (>5%) adverse events at least moderate in severity and with possible, probable or unknown relationship to study drugs.  
 \*\* Adverse events were commonly observed within the first 12 weeks of treatment. In addition, a higher incidence of adverse events was observed at doses greater than 400/400 mg BID.  
<sup>†</sup> One subject (# 2033) discontinued at the end of Year 1; however, this subject experienced an adverse event that continued into Year 2. This subject was considered at risk in Year 2-3.

### Laboratory Abnormalities

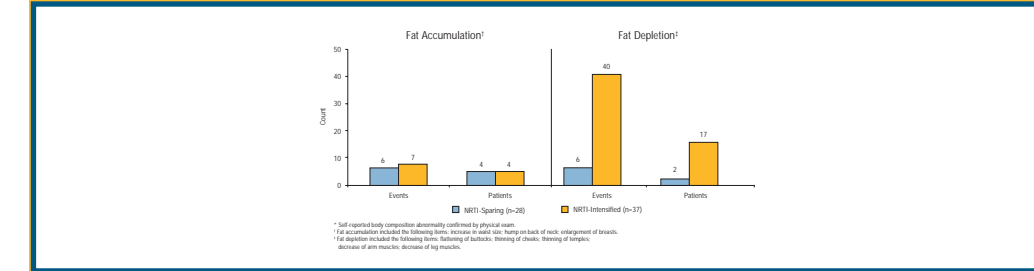
| Laboratory Variable                  | During Year 1 (n = 141) | Subsequent to Year 1 <sup>†</sup> (n = 105) |
|--------------------------------------|-------------------------|---|
| AST (>180 mg/dL) or ALT (>215 mg/dL) | Prevalence 14/141 (10%) | Prevalence 9/105 (9%)                       |
| With baseline liver abnormality*     | 10/51 (20%)             | 5/36 (14%)                                  |
| Without baseline abnormality*        | 4/90 (4%)               | 4/69 (6%)                                   |
| Triglycerides (>750 mg/dL)**         | 35/141 (25%)            | 21/105 (20%)                                |
| Cholesterol (>300 mg/dL)**           | 40/141 (28%)            | 22/105 (21%)                                |

\* Defined as greater than the upper limit of normal for AST/ALT, hepatitis B Ag+ or hepatitis C Ab+ at baseline.  
 \*\* Regardless of fasting or non-fasting conditions.  
<sup>†</sup> Only HIV RNA, CD4 cell count and CD8 cell count were required after Year 2.

### Body Composition Survey

- Administration of a body composition survey completed by subjects at the end of Year 3 and then every 6 months thereafter
- Physical exam for body composition abnormalities conducted at the end of Year 3 and then every 6 months thereafter
- Results have been summarized at the end of Year 5 for each survey item by the proportion of subject-reported, exam-confirmed body composition abnormalities

### Body Composition Survey\* Results at Year 5



### Risk Factor for Body Composition Abnormality\*: Logistic Regression Models

| Risk Factor**                           | Unadjusted Odds Ratio (95% Confidence Interval) | Adjusted Odds Ratio <sup>†</sup> (95% Confidence Interval) |
|---|---|--|
| Intensification with NRTIs <sup>‡</sup> | 4.514 (1.142 – 17.847)                          | 4.710 (1.172 – 18.933)                                     |

\* Defined as at least two body composition abnormalities reported by subject and confirmed by physician.  
 \*\* Other factors including age, gender, baseline HIV RNA, baseline CD4+ cell count, duration of prior RTIs and lipid measurements were not found to be statistically significant for at least two body composition abnormalities.  
<sup>†</sup> Odds ratio adjusted for weight gain (>10%).  
<sup>‡</sup> Intensification with NRTIs occurred in 37/65 (57%) of the subjects.

## CONCLUSIONS

### RTV-SQV — Conclusions at 5 Years

- At year 5, 37.4% (52/139) demonstrated HIV RNA levels <200 copies/mL when randomized to RTV/SQV dual protease inhibitor therapy with or without NRTI intensification (intent-to-treat)
- Through 5 years, 46.1% of subjects (65/141) remained in the study with 52/61 (85%) of subjects on treatment having HIV RNA levels <200 copies/mL and a median increase from baseline of 381 CD4+ cells/mm<sup>3</sup>
- The majority of subjects remaining on study were receiving ritonavir/saquinavir 400/400 mg BID
- Adverse events during Years 4 to 5 were similar in rate and type to those seen during Years 2 to 3
- NRTI-intensification was a significant risk factor for the development of at least two body composition abnormalities, reported by the subject and confirmed by the physician

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