METHODS

Entry Criteria

- Antiretroviral-naive patients

- Plasma HIV RNA > 10,000 copies/mL, with no CD4 cell count restriction

- Patients who had a positive hepatitis B surface antigen (HBsAg) or anti-hepatitis C virus (HCV) antibodies test at screening were excluded from enrollment in Group I and up to 20% of the patients in Group II with a positive HBsAg or anti-HCV antibodies test at screening

Study Design and Analysis

- One hundred antiretroviral-naive patients were randomized to receive one of three dosage levels of LPV/r (200/100 mg BID, 400/100 mg BID or 400/200 mg BID), together with d4T (40 mg BID) and 3TC (150 mg BID) given either after 3 weeks of LPV/r (Group I, n=32) or from study entry (Group II, n=68) (Figure 1).

- Enrollment into Group II began following an evaluation of preliminary efficacy and safety of LPV/r in Group I.

- After 48 weeks, all patients began conversion to open-label LPV/r 400/100 mg BID dosing.

- Plasma HIV RNA was quantified using Roche Amplicor HIV-1 Monitor (lower limit of quantitation [LOQ] 400 copies/mL) and the Roche Amplicor HIV-1 Monitor Ultrasensitive Quantitative PCR, Version 1.0 (LOQ 5 copies/mL).

- CD4 cell counts were measured by flow cytometry.

Antiviral Activity

- Proportion of patients HIV RNA below the limit of quantitation (LOQ) was measured using an on-treatment method (missing values and values obtained during treatment interruptions excluded) and an intent-to-treat, non-complex/future method (ITTF NC-F, mixing values considered failure unless the immediately preceding and following values were below the LOQ).

Virologic Evaluation

- Samples from patients with sustained HIV RNA rebound to >400 copies/mL while receiving LPV/r during the study were submitted for genotypic and phenotypic analyses. Genotypic (GenoType™) and phenotypic (PhenoSense™) analyses were performed by ViRXLogic, Inc.

- Genotypic resistance to LPV was defined as the development of any primary or active site mutation in protease (amino acids 8, 30, 32, 46, 47, 48, 50, 82, 84, and 90) confirmed by phenotypic analyses (≥2 fold increase in IC50 to LPV relative to wild type HIV).

- Resistance to 3TC was defined as the presence of an M184V/I mutation.

Safety

- Cumulative incidence through Week 216 for adverse events and grade 3/4 laboratory values was summarized, as was prevalence at Week 216, defined as the presence of an ongoing adverse event or a grade 3 lab measurement obtained at the Week 216 visit.

- All laboratory measurements were obtained without regard to fasting.

CUNCLUSIONS

- 71% of patients (71/100, ITT NC=F) had HIV RNA <400 copies/mL at Week 216 (on treatment: 99%, 71/72, Figure 6). One patient had HIV RNA = 708 copies/mL at Week 216 following a viral load rebound to >4000 copies/mL at a rate of 5000 copies/mL with no CD4 cell count restriction.

- Viral load suppression below the LOQ

- 17% of patients (17/100, ITT NC=F) had HIV RNA ≤50 copies/mL at Week 216 in treatment, with follow-up HIV RNA values ≤50 copies/mL at Week 228, 240, 252, and 256.

- 70% of patients (70/100, TTF NC=F) had HIV RNA ≤50 copies/mL at Week 204 (on treatment: 97%, 70/72) (Figure 6).

REFERENCES


5. HIV RNA <400 copies/mL


ACKNOWLEDGMENTS

M97-720 Study Subjects

Coordinating Clinical Laboratory Services

• Abbott Laboratories

• Covance Central Laboratory Services AIDS Research Consortium of Atlanta

• J Health-Chiozzi, M King, R King, R Murphy, C Hicks, J Eron, R Glick, M Glesby, P Wolffe, M Thompson, AC White, C Benson, M Albrecht, and S Brum for the M97-720 Study Group.

• Rush Medical College, Northwestern University, Ochsner University Medical Center at University of North Carolina at Chapel Hill.

• Weill Medical College of Cornell University, Pacific Oaks Research, AIDS Research Consortium of Atlanta, Thomas Street Clinic Baylor College of Medicine, University of Colorado, Harvard University, and Abbott Laboratories, USA.
Baseline Characteristics

- Ninety-six male and four female patients: 65% Caucasian, 29% Black, 6% Hispanic.
- Median age: 34 (range 21-55).
- Median Plasma HIV RNA: 4.6 log10 copies/mL (range 3.3-6.2).
- The median CD4 count was 306 cells/mm3 (range 3-918) for all patients and 254 cells/mm3 (range 3-918) for the 72 patients who remained on study for at least 4 years (216 weeks).

Table 1. Patient Disposition at Week 216

<table>
<thead>
<tr>
<th>Disposition</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients enrolled</td>
<td>100</td>
</tr>
<tr>
<td>Patients discontinuing at or before Week 216</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 2. CD4 Cell Count by Baseline CD4 Category

<table>
<thead>
<tr>
<th>Baseline CD4 Cell Count (cells/mm3)</th>
<th>CD4 Change from Baseline (cells/mm3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 (n=16)</td>
<td>458</td>
</tr>
<tr>
<td>50-199 (n=13)</td>
<td>473</td>
</tr>
<tr>
<td>200-349 (n=15)</td>
<td>538</td>
</tr>
<tr>
<td>350-499 (n=12)</td>
<td>498</td>
</tr>
<tr>
<td>≥500 (n=16)</td>
<td>538</td>
</tr>
</tbody>
</table>

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**RESULTS**

Effect of Baseline CD4 and Viral Load on CD4 Cell Count Change from Baseline

- The magnitude of CD4 cell count increase was not significantly correlated with baseline CD4 cell count or baseline viral load (Figures 3a and 3b).

Figure 3a. Effect of Baseline Viral Load on CD4 Count Change from Baseline

- Consistent with a recent report by Hunt et al., patients with the lowest CD4 cell counts at Week 216 (101, 187, and 226 cells/mm3) had the highest T cell activation values (CD38+ HLA-DR+) at the same timepoint (Figure 4).
- However, without these 3 patients, no significant correlation was observed between CD4 activation and Week 216 CD4 cell count (R2=0.037, p=0.13).

Figure 4. Correlation of Activation and CD4 Cell Count at Week 216

- All 72 subjects on study at Week 216 had CD4 cell count increases of at least 99 cells/mm3 (IQR: 322-630, range 99-1657).

Figure 2. CD4 Cell Count Mean Change from Baseline by Baseline CD4 Count

- Among patients with values at both baseline and Week 216, mean (median) CD4 cell count was 793 (738) cells/mm3 at Week 216, a mean (median) increase of 500 (455) cells/mm3.

Table 2. CD4 Cell Count Increase at Week 216 by Baseline CD4 Cell Count

Effect of Baseline CD4 Change by Time Period

- For patients on study at Week 216, increases in CD4 cell count were largest during the first 48 weeks of study. An increase of 141 cells/mm3 was observed during the fourth year of study (Figure 5).

Figure 5. CD4 Count Change by Time Period

- Relationship Between T Cell Activation and Week 216 CD4 Cell Count

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