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# Improvement in Quality of Life with Once-Daily Didanosine-EC (ddI-EC), Lamivudine (3TC), and Efavirenz (EFV): 24 Week Interim Results from the DART I Trial



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## BACKGROUND

The Daily Antiretroviral Therapy (DART I) trial is a Phase IV, 96 week, open label, single arm, prospective multi-center trial designed to assess the efficacy, safety, adherence, and quality of life (QOL) of the once-daily regimen of ddI-EC (400 mg), 3TC (300 mg), and EFV (600 mg) in treatment naive HIV patients. Regimen simplification has been identified as one of many strategies for improving adherence in individuals with HIV.

## METHODS

Inclusion criteria for the study were: Treatment naive subjects with HIV RNA viral load ≥1000 copies/mL by Roche Amplicor HIV-1 assay and CD4 count ≥100 cells/mL obtained within 14 days prior to initiation of therapy, ≥18 years of age, and weight ≥40 kg. Individuals were excluded if pregnant, evidence of hypersensitivity to any study agent, hepatitis or pancreatitis, or failure to fall within acceptable laboratory and clinical parameters. The Medical Outcomes Study HIV Health Survey (MOS-HIV) was utilized to measure QOL. The questionnaire was administered at baseline, 12 and 24 weeks and will continue every 2 months through 96 weeks. The combined Total Well Being and Total Functional Status scores are the sum of 9 domains, while the Overall Total score includes General Health, Change in Health, Total Well Being, and Functional status. Adherence was assessed by both questionnaire and pill counts based on an intent-to-treat (ITT) analysis.

## RESULTS

52 subjects (85% men) with week 24 data were included in the analysis. Cohort demographics, racial distribution, mean baseline HIV RNA level and CD4 cell count are indicated in Table 1. A significant ($p < 0.05$) mean reduction in HIV RNA levels from a baseline of 4.80 $\log_{10}$ copies/mL to 1.70 $\log_{10}$ copies/mL at 24 weeks was observed while a significant ($p < 0.05$) increase in CD4 cell count from 307.6 cells/mm$^3$ at baseline to 498.0 cells/mm$^3$ at 24 weeks was demonstrated. A total of 46 individuals completed QOL questionnaires at 24 weeks. Figure 1 illustrates the significant improvement in Total Well Being at 24 weeks as well as improvement in the Total Functional Status score. Improvement in QOL was seen in virtually all domains (Figure 2) yielding a significant ($p=0.025$) improvement in the Overall Total QOL (Figure 3). At week 24, 88.5% (46/52) of patients responded that they did not miss any dose during the past 4 days on an ITT basis while 85% indicated that they followed their specific dosing schedule (Table 2). Greater than 80% of individuals at week 24 were at least 90% adherent to the once-daily regimen by pill count (Table 3).

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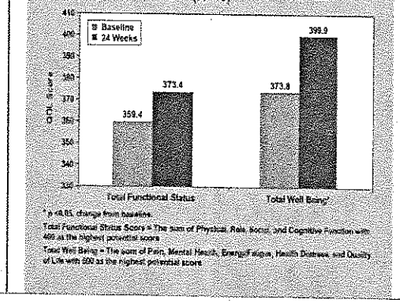
## RESULTS (continued)

**Table 1: Demographics and Baseline HIV RNA Level and CD4 Count**

| | |
|---|---|
| N | 52 |
| Age (mean yrs) | 37 |
| Race: | |
| White | 29 (56%) |
| Black | 16 (31%) |
| Other | 7 (13%) |
| Mean baseline HIV RNA Level ($\log_{10}$ copies/mL) | 4.8 |
| Mean baseline CD4 count (cells/mm$^3$) | 308 |

**Figure 1: Mean MOS-HIV Scores for Total Functional Status and Total Well Being at Week 24 (N=46)**




* $p < 0.05$, change from baseline.

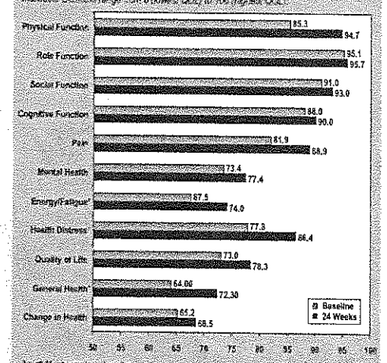
Total Functional Status Score = The sum of Physical, Role, Social, and Cognitive Function with 400 as the highest potential score

Total Well Being = The sum of Pain, Mental Health, Energy/Fatigue, Health Distress, and Quality of Life with 600 as the highest potential score

## RESULTS (continued)

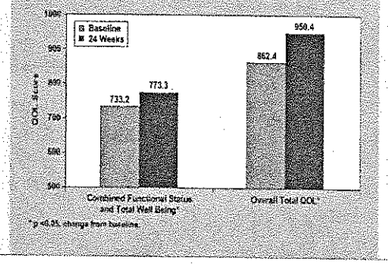
**Figure 2: Mean MOS-HIV Scores for Each Individual QOL Domain at Week 24 (N=46)**

*Individual Domains range from 0 (lowest QOL) to 100 (highest QOL).*




* $p < 0.05$, change from baseline.

**Figure 3: Mean MOS-HIV Scores for Overall Total QOL and Combined Functional Status with Total Well Being (N=46)**




* $p < 0.05$, change from baseline.

## RESULTS (continued)

**Table 2: Adherence Questionnaire Results (N=52 at Week 24)**

| | Proportion of Patients |
|---|---|
| Did not miss any dose during the past 4 days | 88.5% |
| Follow Specific Schedule | 84.8% |
| Followed Instructions over last 4 days | 88.9% |
| At any time took fewer pills per dose: | |
| ddI-EC | 0.0% |
| 3TC | 2.3% |
| EFV | 4.6% |

**Table 3: Proportion of Individuals within Range of Pill Count Adherence (N=52 at Week 24)**

| Adherence Ranges | ≥70% | ≥80% | ≥90% |
|---|---|---|---|
| ddI-EC | 100.0% | 97.8% | 80.0% |
| 3TC | 100.0% | 97.8% | 84.4% |
| EFV | 100.0% | 100.0% | 84.4% |

## DISCUSSION

The QOL gains from initiation of therapy to 24 weeks in this noncomparative trial may be due to the potential psychic benefit achieved through significant reductions in the HIV RNA levels over a relatively short period of time with this simple 3-pill regimen. This can be evidenced by the improvement in the Total Well Being domains and, specifically within the health distress, general health, and energy/fatigue domains.

## CONCLUSIONS

- A high degree of adherence was reported by the patient and also observed through pill counts.
- Significant decreases in HIV RNA levels were demonstrated (mean 3.1 log reduction) along with significant increases in CD4 cell count (mean increase of 189 cells/mm$^3$).
- These data suggest that treatment naive patients experience a significant improvement in their quality of life when initiating a 3-pill QD HAART regimen of ddI-EC, 3TC and EFV.