Low-level Viremia Persists for at Least 7 years in Patients onSuppressive Antiretroviral Therapy

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Background

Persistent viremia can be detected in most HIV-1 infected patients on antiretroviral therapy despite suppression of plasma RNA ≤50 copies/mL. Our previous studies have shown diverse antiretroviral regimens suppress plasma viremia to a new setpoint that correlates with pretherapy viremia. These studies could not detect a significant decline in the viremia setpoint during therapy. We evaluated the persistence of viremia on treatment over 7 years, using a real-time RT-PCR assay with single copy sensitivity.

Study Entry Criteria

- In Study 720, antiretroviral-naive subjects received lopinavir/ritonavir (400/100 mg twice daily) with stavudine and lamivudine twice daily for up to 7 years.
- Subjects remaining on study for 7 years (360 weeks) who never demonstrated detectable viremia (<50 or >400 copies/mL) during weeks 96-360 were included (Figure 2).
- Subjects with comparable baseline assay results (SCA vs. Amplicor) were included in the longitudinal analysis (Figure 3).

Results

- Approximately 76% of samples obtained between weeks 96 and 360 had detectable low-level viremia ranging from 1-39 copies/mL (median 1.7 copies/mL).
- Based on all data from weeks 96-360, a statistically significant decrease in plasma HIV-1 RNA level was observed (half-life=239 weeks, p=0.003, Figure 4).
- However, when data from week 96 were excluded, no decrease in plasma HIV-1 RNA over time was observed (half-life=971 weeks, p=0.83, Figure 5).
- The distributions of individual subject slopes based on all data and on data from weeks 144-360 are displayed in Figure 6.
- Pre-therapy plasma HIV-1 RNA levels were significantly associated with week 96 levels (p=0.002) and week 252 levels (p=0.005) but not with levels at other timepoints (Figure 7).
- No evidence of a change in plasma HIV-1 RNA values was observed in 18 subjects who replaced stavudine with tenofovir DF.
- Median value immediately prior to the switch was 1.37 copies/mL, compared to 1.33 copies/mL 12-24 weeks after the switch (p=0.82, 1-sample t-test).

Conclusions:

These results are consistent with our prior finding that persistent viremia on treatment may originate from virus produced by cells that are infected before initiation of therapy. The apparent biphasic decay in persistent viremia implies that relatively short-lived cells contribute to viremia through 96-144 weeks, and very long-lived cells contribute thereafter. Testing of additional samples between weeks 60-120 may help to elucidate distinctions between phases of decay of persistent viremia.

References: