

Subject category: K

Effect of Early Immunovirologic Discordant Responses on Mortality in Naïve HIV-1 Infected Adults Initiating Treatment in Resource-Constrained Countries

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Background: In therapy-naïve patients, immunological and virological responses at 6 months of combined antiretroviral therapy (cART) are predictors of progression to AIDS or death. In developed countries, immunovirologic discordant responses are associated with an intermediate risk of death, compared to complete and to no response. We previously reported that prevalence of and risk factors for discordant responses in resource-limited settings are similar to those observed in developed countries. In this study, we assessed the impact of immunovirologic patterns of response on mortality in the ART-LINC of IeDEA collaboration.

Methods: All previously naïve participants who initiated cART between 1996 and 2007, were aged 16 years or older, with known date of cART initiation and 6 (3-9) month response were included. Only sites that routinely measured HIV plasma viral load (PVL) were included. The following variables were analyzed: gender, age and clinical stage at CART initiation, site, and 6 (3–9) month responses to therapy, according to virological (PVL<500 copies/mL), and immunological (CD4 cells/mL increase>50) responses, categorized in V+I+, discordant (V+I- or V-I+), and V-I-. Association between independent variables and outcomes were assessed by Cox proportional hazards regression. Robust standard errors were calculated to account for intra-site correlation.

Results: A total of 6,478 patients from 16 sites were included, of which 60.3% were women. The median age was 35 (IQR 30–41) years. The median follow-up time was 1.5 (range 0-8.0) years. 185 deaths occurred during 14,132 person-years of observation (rate 1.41/100py). At 6 (3–9) months, there were 4,498(70.8%) V+I+, 1,020(16.1%) V+I-, 532(8.4%) V-I+, and 297(4.7%) V-I- responses. Multivariable analysis adjusted for age and year of therapy initiation, with complete responders as the reference group, showed that V-

I- patients had the highest risk of death (HR 4.04; 95% CI 2.37–6.85; $p < .001$), followed by discordant responders (HR for V+I- 1.46; 95% CI 1.07–1.99; $p = .01$; and HR for V-I+ 1.63; 95% CI 0.98–2.72; $p = .06$).

Conclusions: Similar to what has been reported from developed countries, in this large cohort of HIV-1 patients from resource-limited countries, immunovirologic discordant responses were associated with intermediate risk of death.