Treatment of primary HIV infection
Grijsen, M.L.

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chapter NINE

Similar virologic response after initiation of triple-class antiretroviral therapy in primary and chronic HIV infection

Marlous L. Grijsen¹, Rebecca Holman², Ferdinand W.N.M. Wit³, Luuk Gras², Selwyn H. Lowe⁴, Kees Brinkman⁵, Frank de Wolf², Jan M. Prins¹

¹Department of Internal Medicine, Division of Infectious Diseases, Center for Infection and Immunity Amsterdam, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands, ²HIV Monitoring Foundation, Amsterdam, the Netherlands, ³Department of Global Health, Amsterdam Institute for Global Health and Development, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands, ⁴Department of Medical Microbiology, Maastricht University Medical Center, Maastricht, The Netherlands, ⁵Department of Internal Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam, the Netherlands

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Abstract
We compared the time to viral suppression between a cohort of 70 primary HIV infected (PHI-) patients treated with triple-class therapy and a cohort of 80 naive chronic HIV infected (CHI-) patients with comparable treatment and plasma viral load (≥100,000 copies/ml) at start of cART. The time to viral suppression after initiation of triple-class therapy was comparable for PHI and CHI, suggesting that the virologic response to therapy is not related to the stage of HIV infection.
Studies comparing the virologic response to cART between persons with primary (PHI) and chronic HIV infection (CHI) have shown inconsistent results [1-5]. In a recent issue of this journal, a more rapid plasma viral load (pVL) decline was observed in PHI as compared to CHI after initiation of a standard NNRTI-based regimen [1]. We compared the time to viral suppression in our cohort of 70 PHI-patients treated with triple-class therapy with that of 80 naïve CHI-patients with comparable treatment and initial pVL.

PHI-patients were selected from the Primo-SHM cohort, a prospective cohort study in the Netherlands with an embedded randomized trial which investigated the effects of 24 or 60 weeks of cART during PHI [6]. PHI was defined as a negative or indeterminate Western blot combined with a detectable pVL, or, in case of a positive Western blot, a negative HIV screening test result ≤ 180 days. CHI-patients were selected from the Dutch observational HIV cohort (ATHENA) [7]. Inclusion criteria for PHI- and CHI-patients in the present study were: age ≥18 years, treatment-naïve, a pVL of ≥100.000 c/ml, and start of triple-class cART between January 2002 and June 2010.

Time to viral suppression, defined as a pVL <50 c/ml, was compared between the two cohorts using Kaplan-Meier plots and multivariate Cox regression analysis, the last adjusted for the pVL before treatment and regimens containing an integrase inhibitor. Analyses were intention-to-treat, regardless of treatment changes. Patients were censored when lost-to-follow-up or when cART was interrupted for more than two weeks. Chi-squared, Fisher’s exact and Kruskal-Wallis tests were used where appropriate.

Sixty-four of 70 PHI-patients (91%) and 72 of 80 CHI-patients (90%) were men (P=0.8). The PHI-patients were younger (median age 38 (IQR 31-45) versus 42 (36-49) years; P=0.02), were more often men who have sex with men (59 (84%) versus 50 (63%); P=0.003), and had a higher median CD4 count prior to treatment than CHI-patients (470 (IQR 300-550) versus 97 (39-215) cells/mm³; P<0.001). Median baseline pVL was similar in both groups: 5.7 (IQR 5.3-6.1) versus 5.7 (5.4-6.1) log₁₀ c/ml (P=0.4). Fifty-seven PHI-patients (81%) had a negative or indeterminate Western blot, 67 (96%) were symptomatic during PHI, and the median time between HIV diagnosis and start of early cART was 4 (IQR 3-7) weeks. Twenty-nine CHI-patients (36%) had experienced a CDC-C event before treatment initiation.

All 70 PHI-patients and 69 of 80 CHI-patients (86%) initiated a triple-class regimen containing two NRTIs, an NNRTI and a boosted PI. The remaining 11 CHI-patients (14%) received an integrase inhibitor in addition to two NRTIs plus an NNRTI (n=5) or boosted PI (n=6). HIV genotyping was available for 111 patients (74%): three of 54 PHI- (6%) and six of 57 CHI-patients (11%; P=0.5) harboured one or more transmitted drug resistance mutations in reverse transcriptase or protease [8], of whom one PHI-patient and two CHI-patients were judged as being treated with an ineffective triple-class regimen and therefore excluded from further analyses.

A total of 47 of 69 PHI-patients (68%) and 59 of 78 CHI-patients (76%) switched to an alternative or simplified regimen before 24 weeks (P=0.3). Median time to viral suppression was comparable between both groups (log-rank, P=0.5; Figure 1). This was confirmed by the adjusted Cox regression analysis (HR PHI versus CHI 1.08 (95% CI 0.74-1.58), P=0.7). After 24 weeks 50% of the patients in both groups had a pVL ≤50 copies/ml, and after 48 weeks this was 82% in PHI- and 93% in CHI-patients.
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Figure 1. Kaplan-Meier curves of the probability of achieving a viral suppression. Kaplan-Meier curve of the probability to achieve viral suppression (pVL <50 copies/ml) for primary and chronic HIV-infected patients with a high viraemia (pVL >100.000 copies/ml) initiating triple-class therapy.

The time to viral suppression in PHI was comparable to CHI after initiation of triple-class therapy. This is in contrast with a recent report, in which phase II viral decay was faster in PHI than in CHI, which resulted in a shorter time to viral suppression after start of treatment with dual-class, NNRTI-based therapy [1]. A much smaller study, which was designed to assess the effect of raltegravir on viral dynamics, also demonstrated a faster time to viral suppression in PHI than in CHI, but did not adjust for the higher baseline pVL in the CHI-patients [2]. In contrast to our study, both latter studies compared patients receiving standard triple therapy [1, 2], and the question is whether this explains why these two studies found a difference between PHI- and CHI-patients. A prospective cohort study observed that PHI-patients receiving quadruple dual-class therapy had a faster phase II viral decay and a non-significant shorter time to viral suppression than PHI-patients on triple therapy [9]. However, it is not clear how this differential effect of the regimen on HIV suppression should explain a shorter time to viral suppression in PHI- versus CHI-patients for dual-class [1], as opposed to triple-class therapy.

In summary, our results demonstrate that PHI- and CHI-patients with high viraemia are equally rapidly suppressed after initiation of triple-class therapy, suggesting that the virologic response to cART is not related to the stage of HIV infection.

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Contributors
MLG and JMP conceived the study. RH, LG and FWNMW conducted the statistical analysis. MLG and JMP provided valuable input into interpretation of data. MLG drafted the manuscript and JMP critically revised the manuscript. All authors reviewed and approved the final version of the manuscript.
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