Long-term virological response to multiple sequential regimens of highly active antiretroviral therapy for HIV infection

Gilbert R Kaufmann, Nina Khanna, Rainer Weber, Luc Perrin, Hansjakob Furrer, Matthias Cavassini, Bruno Ledergerber, Pietro Vernazza, Enos Bernasconi, Martin Rickenbach, Bernard Hirscher, Manuel Battegay & Swiss HIV Cohort Study

OBJECTIVE: Information about the virological response to sequential highly active antiretroviral therapy (HAART) for HIV infection is limited. The virological response to four consecutive therapies was evaluated in the Swiss HIV Cohort. DESIGN: Retrospective analysis in an observational cohort. METHODS: 1140 individuals receiving uninterrupted HAART for 4.8 +/- 0.6 years were included. The virological response was classified as success (<400 copies/ml), low-level (LF: 400-5000 copies/ml) or high-level failure (HF: >5000 copies/ml). Potential determinants of the virological response, including patient demographics, treatment history and virological response to previous HAART regimens were analysed using survival and logistic regression analyses. RESULTS: 40.1% failed virologically on the first (22.0% LF; 18.1% HF), 35.1% on the second (14.2% LF; 20.9% HF), 34.2% on the third (9.9% LF; 24.3% HF) and 32.7% on the fourth HAART regimen (9% LF; 23.7% HF). Nucleoside pre-treatment (OR: 2.34; 95% CI: 1.67-3.29) and low baseline CD4 T-cell count (OR: 0.79/100 cells rise; 95% CI: 0.72-0.88) increased the risk of HF on the first HAART. Virological failure on HAART with HIV-1 RNA levels exceeding 1000 copies/ml predicted a poor virological response to subsequent HAART regimens. A switch from a protease inhibitor- to a non-nucleoside reverse transcriptase inhibitor-containing regimen significantly reduced the risk of HF. Multiple switches of HAART did not affect the recovery of CD4 T lymphocytes. CONCLUSION: Multiple sequential HAART regimens do not per se reduce the likelihood of long-term virological suppression and immunological recovery. However, early virological failure increases significantly the risk of subsequent unfavourable virological responses. The choice of a potent initial antiretroviral drug regimen is therefore critical.