Reference curves for CD4 response to antiretroviral treatment in HIV-1 infected naive patients

Rodolphe Thiebaut on behalf of the Standard Reference distribution of CD4 response to HAART Project Team for the Collaboration of Observational HIV Epidemiological Research Europe (COHERE) in EuroCoord

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Background & Objective

- The primary virological goal of combination antiretroviral treatment (cART) is the attainment of an undetectable viral load as soon as possible after cART initiation, usually in the first 6 months.
- AIDS virological response, however, is less clearly defined.
- The risk of clinical progression is more strongly associated with the absolute CD4 count at a given time than the rate of increase in the CD4+ T cell count.
- Reference curves may help in the management of patients.

Objective: To provide ‘reference curves’ for CD4+ T cell responses during the first 12 months of cART for patients with virological suppression and according to different characteristics at cART initiation.

Methods

Population
- Cohorts participating in the COHERE Collaboration, a collaboration of 39 European observational cohorts of HIV-infected individuals.
- Age 18 years.
- First cART started from 1/1/2005 to 1/1/2010.
- At least one available CD4 count (in cells/µL).
- HIV RNA ≤ 50 copies/mL.
- ART regimen: constraining at least three drugs, including a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), an entry inhibitor, or containing abacavir +1 nucleoside reverse-transcriptase inhibitors.

Statistical analysis
- A prior stratification factors: baseline CD4+ T cell count, AIDS clinical stage, age, HIV transmission group, CD4 T cell RNA level, year of cART initiation and type of cART.
- Quantile regression on repeated measurements of CD4+ T cell count available for each individual until 9 months and then until 15 months.
- Models adjusted for time with squared and cubic effects to fit a nonlinear evolution of CD4 over time.
- Models fitted after including adjustment for the covariates listed above; this set of models can be used to make predictions for individual responses taking into account individual characteristics.
- Models fitted using SAS v9.3 PROC QUANTREG. Robustness analyses with median regression including a random intercept to take into account correlation (1).

Results

Population characteristics: N=28,992 individuals
- Median (interquartile range [IQR]) age at cART initiation: 39 (33-46) years.
- 8% Hepatitis C Virus positive.
- Median (IQR) CD4+ T cell count at ART initiation: 292 (181, 427) cells/µL.
- 2.4% (1.7% abacavir, 0.5% Integrase inhibitor, 0.08% fusion inhibitor, 0.05% other combination).
- 350-499: 14%.
- Both PI and NNRTI: 1%
- Unboosted PI: 2%
- ≥ 50 copies/mL at least one available CD4 count (in cells/µL).
- 53 percentile (86 percentile, 45 percentile). 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentile, 5th percentile, 10th percentil...