What frequency of monitoring is needed for health-care in an HIV-infected person?

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INTRODUCTION

Current guidelines recommend that patients on combination antiretroviral therapy (cART) visit clinics on a three monthly basis, for monitoring treatment together with testing of viral load, CD4 cell count, liver and renal function tests, lipid profiles and glucose levels. Previous studies have shown that the greatest risk of treatment failure is in the first few months after starting treatment and that the risk of clinical disease progression (new AIDS/death) is significantly higher in patients with low CD4 counts and those who can not maintain an undetectable viral load. It might be possible to monitor patients who are stable on their current cART regimen less frequently, which would be advantageous for both patient and clinic.

AIMS

• Assess whether patients on a stable and fully suppressed cART regimen could be monitored less frequently
• Determine the increased risk of cART treatment failure with less frequent monitoring

METHODS

Patients

2082 patients on a stable and fully suppressed cART regimen for a period of one year within EuroSIDA. cART was defined as a regimen of at least 3 drugs, of which at least 2 were nucleosides/nucleotides (NRTI) and one was a non-nucleoside (NNRTI) or a protease inhibitor (PI). A stable and fully suppressed regimen was defined as a period of 1 year with:

• Maximal viral suppression (all HIV-RNA in 12 month period < 500 copies/ml; >2 measurements required)
• All measured CD4 counts > 1000/mm3 (2 measurements required)
• A minimum CD4 count increase after starting cART of 100/mm3
• No changes to cART regimen in the previous 12 months
• No new or existing illness or non-nAIDS defining malignancies in 12 month period
• No other serious morbidity (CVD, diabetes, hypertension, grade III/IV liver failure) diagnosed 12 month period

Statistical Methods

Baseline was defined as the end of the 12 month period after satisfying the inclusion criteria above. Kaplan Meier estimation was used to find the probability of failure in the 3, 6 or 12 months after baseline. Failure was defined as:

• Any of the above
• Univariate and Multivariate Cox proportional hazards models, stratified by centre, were used to determine which factors were related to failure.

RESULTS

Baseline characteristics are described in table 1. 1054 patients (50.6%) were ARV-naïve at starting cART and 928 (47.7%) had a prior diagnosis of AIDS. Median CD4 nadir was 518/mm3 (IQR 67, 253), median CD4 at starting cART 220/mm3 (IQR 150, 350), median viral load at starting cART 4.63 log10 copies/ml (IQR 3.79, 5.73), and median peak viral load 4.9 4 log10 copies/ml (IQR 4.53, 5.42).

Of the 2082 patients in this study, 126 patients (6%) failed for any reason in the first year after baseline.

• Figure 1 shows the percentage of a patients failing each of the failure categories
• Figure 2 shows the Kaplan Meier plot of the risk of failure in the first 12 months after baseline

There was an estimated 0.3%, (95% CI 0.1,0.5), n=7, probability of cumulative failure within 3 months, increasing to 2.2% (1.9,3.7), n=2, 6% (3.5,7.4), n=1, after 12 months respectively.

The main reason for failure was viral rebound, with an estimated 4.9% (95% CI 4.0,5.8) with viral rebound after 12 months. The individual risk of deterioration of immune function, new morbidity (AIDS or non-AIDS) or death, were all less than 1% over 12 months.

The results of the multivariate model are shown in table 2:

• Increased risk of failure in female patients, decreased risk of failure if patients were on a NNRTI regimen compared to a single-PI regimen, however these were only marginally significant
• Increased risk of failure in patients with more time spent with unsuppresses viremia prior to baseline
• A patient was 7 times more likely to fail if they stopped or decreased the number of ARVs they were taking

Figure 3 shows the reduced risk of treatment failure in patients who have spent less than 6 months with uncontrolled viremia and on a NNRTI based cART, with patients censored if they reduce or stopped taking ARVs. Of the 2082 patients, 941(45.2%) fitted this criteria and after 12 months of follow-up 35 patients had failed (3.7%) and 89 were still under follow-up. In this subgroup of patients, the proportion of patients estimated to have failed at 6 months was 1.3% (95% CI 0.6,2.0) and 3.6% (95% CI 3.4,4.8) after 12 months.

CONCLUSIONS

Patients who have responded well to cART and are on a well tolerated and fully suppressive cART regimen, provided they have experienced extended periods, of at least a year, with complete viral suppression and if the regimen contains a NNRTI, have a low chance of failure of cART for the next 3-6 months. Therefore in this subgroup of otherwise healthy patients it may be reasonable to extend visit intervals to 6 months, with cost and time savings to both the treating clinics and the patients.