Opportunistic infections in immunocompromised but virologically suppressed HIV-1 infected patients


for the EuroSIDA study group

BACKGROUND

- A low CD4 count and a high viral load (VL) are associated with clinical progression to AIDS or death.
- Limited knowledge of the relative risk in patients with a low CD4 count and a suppressed VL.
- There may be different predictors of disease progression and death specific to these particular patients compared to those with unsuppressed VL.

AIMS

- To compare the incidence of opportunistic infections (OIs) and death in immunocompromised patients with a CD4 count ≤ 200 cells/mm³ between those with:
  - VL <500 copies/mL whilst on antiretroviral therapy (cART): VL<500 on cART
  - VL >500 copies/mL whilst on cART: VL>500 on cART

- To compare the incidence of opportunistic infections (OIs) and death in immunocompromised patients with a CD4 count ≥ 200 cells/mm³ between those with:
  - VL <500 copies/mL whilst off all ART: VL<500 no ART
  - VL >500 copies/mL whilst off all ART: VL>500 no ART

INCLUSION CRITERIA

- Patients were included who:
  - ≥ 1 month’s prospective follow-up with a CD4 count ≥ 200 cells/mm³ after Jan 1997
  - ≥ 0.2 CD4 counts were measured within 6 months before the CD4 count

METHODS

- CART was defined as at least 3 drugs including a PI, NNRTI or abacavir

- PYFU were split into 3 groups according to most recent VL and treatment

- PYFU contributed by a patient were not necessarily consecutive and a patient could be included in more than one group

- Incidence rates of OIs and death were calculated as number of events per 100 PYFU

- Multivariable Poisson regression models were used to determine the predictors of OIs and death, adjusted for repeated events per patient

RESULTS

- 4,924 patients were included: 3,164 patients with VL<500 on cART, 3,537 with VL>500 on cART and 1,601 with VL>500 no ART

- 7,686 PYFU were included: 3,225 PYFU with VL<500 on cART, 3,624 with VL>500 on cART and 877 with VL>500 no ART

- 70% of PYFU were from white males, 41% homosexual, 25% injecting drug users and 25% heterosexual

- CD4 counts were lowest in PYFU with VL>500 on cART (96 ± 2,000 cells/mm³) and highest in VL<500 on cART (99 ± 2,000 cells/mm³)

- Viral loads were highest in VL<500 on cART (89 ± 2,000 copies/mL compared to 63% in VL>500 on cART)

- Patients started CART a median time of 2.7 (IQR: 2.2-4.1) years prior to first VL<500 on cART and 2.0 (IQR: 1.9-3.6) years prior to first VL>500 on cART

- Of 3,624 patients with VL>500 on cART, 1,345 (38%) had previously had VL suppression a median time of 8 (IQR: 4-19) months before first VL<500 on cART

- 626 patients (29%) with VL>500 no ART had never started CART and 265 (13%) had never started CART. Among those that had, the median time since stopping CART was 2.0 (IQR: 0.4-5.2) months

- The overall incidence of OIs and death was found to be lowest in the VL<500 on cART group: 5 events per 100 PYFU

- Figure 1 shows the incidence rate ratios of OIs and deaths. After adjustment for the variables listed in the figure, the rate of OIs in VL<500 on cART was significantly and almost twice that of VL>500 on cART. The patient-off-treatment had a rate 4.5 times that of VL>500 on cART. Overall death rates in VL>500 on cART were nearly as high as that of VL<500 on cART. However, the rate in VL>500 on cART was slightly lower

- Figure 2 shows that this was a lower rate of non HIV-related deaths in VL<500 on cART that had resulted in the unexpected lower overall death rate. The rate of HIV-related deaths in VL>500 on cART was higher than that in VL<500 on cART after adjustment, although not significantly

- A sensitivity analysis was carried out excluding deaths that occurred within 3 months of stopping treatment. In VL>500 no ART this reduced the HIV-related death rate ratio to 1.8 and the non HIV-related death rate ratio to 3.4

- A further sensitivity analysis defined a group VL>500 on cART, VL<500 on cART and VL<500 no ART taking only PYFU in which the viral load was used to define a limit of detection 50, leaving a total of 6655 PYFU. Similar patterns were observed with VL<500 on cART having the lowest rate of OIs. HIV death rates were similar between the first three groups all on CART. The non HIV death rate was lowest in VL>500 no ART

CONCLUSIONS

- Achieving full VL suppression in immunocompromised patients with a CD4 count ≥ 200 cells/mm³ is important for reducing the risk of OIs

- Use of CART in patients with unsuppressed VL also reduces the risk, suggesting a beneficial effect over and above what can be explained by suppression of VL and increases in CD4 count

- Patients on CART have a much lower risk of death than those not receiving CART, regardless of VL suppression

- Part of this difference in risk of death was due to terminally ill patients being taken off CART and part was due to non HIV-related deaths

- Non HIV-related death rate was lower in those with an unsuppressed VL on CART compared to a suppressed VL. Further investigation into competing risks and specific causes of death is needed to explain this