#316

Plasma levels of soluble CD163 predict all-cause mortality from HIV-1 infection

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Background

CD163, a monocyte- and macrophage-specific scavenger receptor, is shed from the cell surface as soluble CD163 (sCD163) in response to inflammatory stimuli. Here, we assessed the association of sCD163 levels in HIV-1 infection and all-cause mortality.

Methods

Plasma sCD163 levels were measured by ELISA in a HIV-1 infected prospective cohort (n=923) followed for 8.4 years. A substudy (n=25) investigated sCD163 changes during 24 weeks of antiretroviral treatment (ART). Hazard rates (HR) with 95% confidence intervals (95% CI) associated with mortality were calculated using adjusted Cox proportional hazards regression analysis.

Figure 1. Kaplan Meier plot showing the difference in survival for 923 HIV-1 infected patients followed for 8.4 years with sCD163 levels stratified by 0-30, 31-60, 61-90 and 91-100 percentiles (Log-rank: p<0.0001)

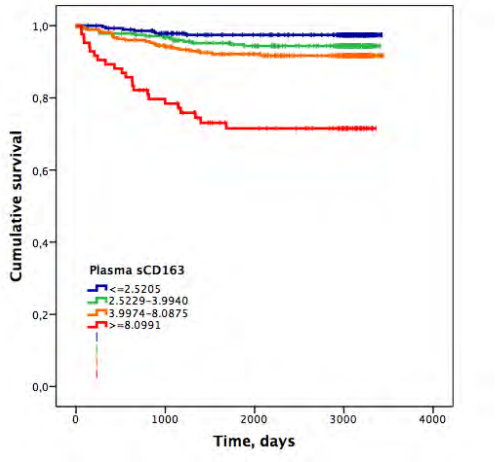


Table 1. Baseline clinical and demographic characteristics of the Hvidovre Clinic Cohort

	Hvidovre Clinic Cohort N=923
Age, years	42 (37-50)
Males, %	664 (72%)
Blood CD4 T cell, count cells/µl	505 (351-703)
Plasma HIV RNA, copies/ml	<20 (<20-74)
Plasma sCD163, mg/l	3.39 (2.27-5.07)
ART at inclusion, (%)	791 (86%)
Time on ART at inclusion, years	6.0 (3.5-7.6)
Transmission group	
MSM	408 (44%)
HSX	323 (35%)
IDU	137 (15%)
Other	55 (6%)
Follow up time, years	8.3 (6.0-8.8)
Death during follow up, %	67 (7.3%)

All values median and interquartile range.
sCD163: soluble CD163; MSM: men who have sex with men; HSX: heterosexual; IDU: injecting drug use

Table 2. Multivariate analysis of risk of death during follow in the Hvidovre Clinic Cohort

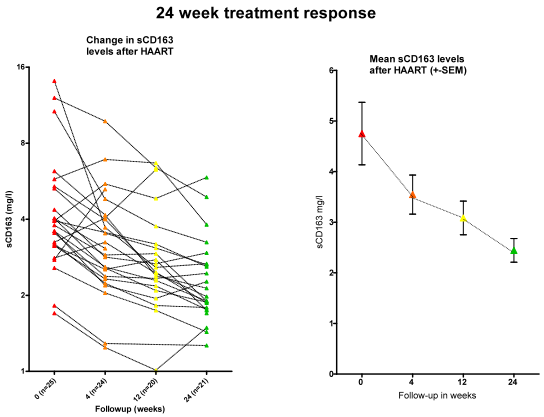
Variable	Crude HR (95% CI)	Adjusted HR (95% CI)	Adjusted HR (95% CI)
sCD163, per mg/L increment	1.11 (1.09-1.13)	1.09 (1.05-1.12)	1.18 (1.11-1.25)
Age, per year increment	1.05 (1.03-1.08)	1.08 (1.05-1.10)	1.08 (1.06-1.12)
Sex			
Male	1.0	1.0	1.0
Female	0.86 (0.50-1.49)	1.03 (0.56-1.89)	1.01 (0.55-1.85)
IDU			
No	1.0	1.0	1.0
Yes	3.67 (2.24-6.03)	2.34 (1.29-4.25)	2.36 (1.30-4.30)
Log HIV RNA, per log increment	1.37 (1.17-1.61)	1.18 (0.96-1.46)	0.84 (0.59-1.19)
CD4 T cell count per doubling	0.62 (0.53-0.73)	0.64 (0.51-0.80)	0.58 (0.45-0.76)
ART at study inclusion			
No	1.0	1.0	-
Yes	0.74 (0.40-1.39)	1.29 (0.57-2.89)	
ART, time-updated			
No	1.0	-	1.0
Yes	0.53 (0.27-1.05)		0.61 (0.27-1.39)

HR: hazard ratio; CI: confidence interval; sCD163: soluble CD163; IDU: injecting drug use; ART: antiretroviral treatment

Results

In 2004-05, 923 consecutive individuals had plasma sCD163 measured. During 8.4 years of follow up there were 67 deaths (table 1). The cumulative incidence of death increased with increasing plasma sCD163 levels (figure 1). By multivariate Cox analysis, there was a 9% increased risk of death for each mg increase in baseline plasma sCD163 (aHR: 1.09 (95% CI: 1.05-1.10)). In time-updated analysis of antiretroviral treatment (ART) status, the risk of death associated with baseline levels of plasma sCD163 increased to 18% per mg increase (aHR: 1.18 (95% CI: 1.11-1.25)). Age, injecting drug use (IDU) and blood CD4 T cell counts were also associated with death (Table 2). In the substudy the mean plasma sCD163 levels declined significantly from 4.8 mg/L to 2.4 mg/L over 24 weeks after initiation of ART (figure 2).

Figure 2. Plasma soluble CD163 changes over 24-weeks after initiation of ART. Individual measurements are shown on the left and mean values with standard errors on the right



Conclusion

- Plasma sCD163 is an independent marker of all-cause mortality in a cohort of HIV-1 infected individuals.
- sCD163 levels decline significantly after initiation of antiretroviral treatment.
- Measurement of sCD163 may be useful for monitoring and identifying individuals at risk of developing fatal complications.

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