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Short term clinical disease progression in HIV-1 positive patients taking combination antiretroviral therapy: The EuroSIDA risk-score

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BACKGROUND

- Predicting HIV clinical progression using prognostic scores normally concentrates on predicting long-term clinical progression based on information known at starting cART
- It could be clinically more relevant to accurately assess the risk of clinical progression in the next 3 or 6 months at any time after starting cART, based on the laboratory results currently known

OBJECTIVES

- To develop a EuroSIDA risk-score to predict the short term risk of clinical progression (new AIDS or death)
- To validate this score in the Swiss HIV Cohort Study (SHCS)

PATIENTS (N=3338)

- Patients starting cART (defined as exactly 2 nucs, plus either a single PI, a ritonavir-boosted PI, NNRTI, or abacavir) with CD4/VL measured before starting cART
- Haemoglobin and BMI measured during follow-up

METHODS

- Poisson regression, all variables included as time-updated

THE EUROSIDA RISK SCORE

- 616 new AIDS/deaths during 18,203 PYFU
- CD4, rate of change of CD4, VL, BMI, level of anaemia, prior ARV treatment, and current ARV treatment were related to clinical progression
- EuroSIDA risk-score shown in Figure 1
- Example shown in Figure 2

A single unit increase in the current EuroSIDA risk-score was associated with a 2.70 times higher incidence of clinical progression (95% CI 2.57 – 2.85, p<0.0001)

The EuroSIDA risk-score was divided into 4 groups; <1.5, 1.5-2.99, 3-4.49 and ≥4.5. Figure 3 illustrates the chance of clinical progression within the next 3, 6 or 12 months after a clinic visit, within these 4 strata.

VALIDATION IN THE SHCS

- 4,700 patients from the SHCS satisfied the inclusion criteria and were included as the validation cohort

Figure 4 illustrates the incidence rates of new AIDS/death after stratification by current EuroSIDA risk-score in both EuroSIDA and the SHCS

In the SHCS patients, a single unit increase in the current EuroSIDA risk-score was associated with a 2.84 times higher incidence rate of clinical progression (95% CI 2.71–2.99, p<0.0001)

CONCLUSIONS

- Current CD4, viral load, level of anaemia, BMI, and rate of CD4 change were highly prognostic for new AIDS/death
- A risk-score was derived and validated on SHCS patients with good agreement
- A patient with a EuroSIDA risk-score of less than 1.5 had a 1 in 629 chance of disease progression within the next 3 months, compared to a chance of 1 in 12 for a patient whose EuroSIDA risk-score was over 4.5
- The EuroSIDA risk-score will be made publicly available on a website where relevant details can be entered and the score calculated without the need for clinicians to calculate the CD4 slope
- The EuroSIDA risk-score is highly clinically relevant for patient management, or for use as a surrogate endpoint in clinical trial design.

Figure 1

The EuroSIDA risk-score

	If current (latest)		*If current (latest)*
+0	CD4 > 350/mm³	+0.54	BMI ≤18
+0.61	CD4 201-350/mm³	+0	BMI 18.1-25
+1.55	CD4 51-200/mm³	-0.29	BMI > 25
+2.53	CD4 ≤ 50/mm³		
		+0.48	CD4 slope< -25/mm³ per 3 months
+0	Viral load < 500 copies/ml	+0	CD4 slope -25 to +25/mm³ per 3 month
+0.15	Viral load ≥ 500 copies/ml	+0.20	CD4 slope> 25/mm³ per 3 months
+0	No anaemia	+0	If ARV experienced prior to cART
+0.78	Mild anaemia	-0.34	If ARV naïve prior to cART
+2.05	Severe anaemia		
		+0	Taking any antiretrovirals
+0.024	x age (in years)	+1.24	Off all antiretrovirals

Figure 2

Example of EuroSIDA risk-score

- 30 year old patient
- Started cART from ARV naïve
- Current CD4 count 400/mm³, viral load 50 copies/ml
- Currently BMI of 22 and mild anaemia
- CD4 slope increased by 15/mm³ over the past 3 months
- Currently taking cART

EuroSIDA risk-score = 1.16

0 *(CD4 component)* + 0 *(viral load component)* + 0.78 *(mild anaemia)* + 0 *(BMI component)* + 0.024*30 *(age)* + 0 *(CD4 slope component)* + 0 *(on cART)* + 0 *(ARV experienced)*

Figure 3

Clinical progression according to EuroSIDA risk-score

		Chance of New AIDS/Death	95% Confidence Interval
Within 3 months			
EuroSIDA	<1.5	1 in 607	1 in 477 to 1 in 834
Risk-score	1.5 – 2.99	1 in 185	1 in 161 to 1 in 218
	3.0 – 4.49	1 in 42	1 in 36 to 1 in 49
	≥ 4.5	1 in 13	1 in 12 to 1 in 15
Within 6 months			
EuroSIDA	<1.5	1 in 304	1 in 239 to 1 in 417
Risk-score	1.5 – 2.99	1 in 93	1 in 81 to 1 in 109
	3.0 – 4.49	1 in 21	1 in 18 to 1 in 25
	≥ 4.5	1 in 7	1 in 6 to 1 in 8
Within 12 months			
EuroSIDA	<1.5	1 in 152	1 in 120 to 1 in 209
Risk-score	1.5 – 2.99	1 in 47	1 in 41 to 1 in 55
	3.0 – 4.49	1 in 11	1 in 9 to 1 in 13
	≥ 4.5	1 in 4	1 in 3 to 1 in 5

Figure 4

Incidence of new AIDS/death stratified by current EuroSIDA risk-score

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